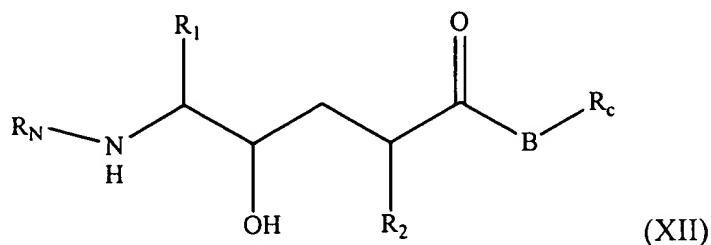


WE CLAIM:

1. A method for inhibiting  $\beta$ -secretase activity, comprising exposing said  $\beta$ -secretase to an effective inhibitory amount of a hydroxyethylene compound of the formula



where  $R_1$  is:

- (I)  $C_1$ - $C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, - $NH_2$ , -C $\equiv$ N, -CF $_3$ , or -N $_3$ ,
- (II) -(CH $_2$ ) $_{1-2}$ -S-CH $_3$ ,
- (III) -CH $_2$ -CH $_2$ -S-CH $_3$ ,
- (IV) -CH $_2$ -(C $_2$ -C $_6$  alkenyl) unsubstituted or substituted by one -F,
- (V) -(CH $_2$ ) $_{0-3}$ -(R $_{1-aryl}$ ) where R $_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:
  - (A)  $C_1$ - $C_3$  alkyl,
  - (B) -CF $_3$ ,
  - (C) -F, Cl, -Br and -I,
  - (D)  $C_1$ - $C_3$  alkoxy,
  - (E) -O-CF $_3$ ,
  - (F) -NH $_2$ ,
  - (G) -OH, or
  - (H) -C $\equiv$ N,
- (VI) -(CH $_2$ ) $_{n_1}$ -(R $_{1-heteroaryl}$ ) where  $n_1$  is 0, 1, 2, or 3 and R $_{1-heteroaryl}$  is:
  - (A) pyridinyl,

- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyl,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thienyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,

- (GG) 1, 4-benzodioxan
- (HH) purinyl,
- (II) oxazolopyridinyl,
- (JJ) imidazopyridinyl,
- (KK) isothiazolyl,
- (LL) naphthyridinyl,
- (MM) cinnolinyl,
- (NN) carbazolyl,
- (OO)  $\beta$ -carbolinyl,
- (PP) isochromanlyl,
- (QQ) chromanyl,
- (RR) furazanyl,
- (SS) tetrahydroisoquinoline,
- (TT) isoindolinyl,
- (UU) isobenzotetrahydrofuranyl,
- (VV) isobenzotetrahydrothienyl,
- (WW) isobenzothiophenyl,
- (XX) benzoxazolyl, or
- (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1$ - $C_3$  alkoxy,
- (5)  $-O-CF_3$ ,
- (6)  $-NH_2$ ,
- (7)  $-OH$ , or
- (8)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $-(CH_2)_{n_1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and

$R_{1\text{-heterocycle}}$  is:

- (A) morpholinyl,
- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2)  $C_1$ - $C_3$  alkyl,
- (3)  $-CF_3$ ,
- (4) -F, Cl, -Br and -I,
- (5)  $C_1$ - $C_3$  alkoxy,
- (6)  $-O-CF_3$ ,
- (7)  $-NH_2$ ,
- (8) -OH, or
- (9)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $R_2$  is:

- (I) -H,
- (II)  $C_1-C_6$  alkyl, or
- (III)  $-(CH_2)_{0-4}-R_{2-1}$  where  $R_{2-1}$  is  $(C_3-C_6)$ cycloalkyl,  $R_{1-aryl}$  or  $R_{1-heteroaryl}$

where  $R_{1-aryl}$  and  $R_{1-heteroaryl}$  are as defined above,

where  $R_N$  is:

(I)  $R_{N-1}-X_N$ - where  $X_N$  is:

- (A)  $-CO-$ ,
- (B)  $-SO_2-$ ,
- (C)  $-(CR'R'')_{1-6}$  where  $R'$  and  $R''$  are the same or different and are  $-H$  or  $C_1-C_4$  alkyl,
- (D)  $-CO-(CR'R'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is  $-O-$ ,  $-S-$  and  $-NR'R''-$  and where  $R'$  and  $R''$  are as defined above,
- (E) a single bond;

where  $R_{N-1}$  is:

(A)  $R_{N-aryl}$  where  $R_{N-aryl}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1)  $C_1-C_6$  alkyl,
- (2)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (3)  $-OH$ ,
- (4)  $-NO_2$ ,
- (5)  $-CO-OH$ ,
- (6)  $-C\equiv N$ ,
- (7)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are:
  - (a)  $-H$ ,
  - (b)  $-C_1-C_6$  alkyl unsubstituted or substituted with one
    - (i)  $-OH$ , or

- (ii)  $\text{-NH}_2$ ,
- (c)  $\text{-C}_1\text{-C}_6$  alkyl unsubstituted or substituted with one to three  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ , or  $\text{-I}$ ,
- (d)  $\text{-C}_3\text{-C}_7$  cycloalkyl,
- (e)  $\text{-(C}_1\text{-C}_2\text{ alkyl)-(C}_3\text{-C}_7\text{ cycloalkyl)}$ ,
- (f)  $\text{-(C}_1\text{-C}_6\text{ alkyl)-O-(C}_1\text{-C}_3\text{ alkyl)}$ ,
- (g)  $\text{-C}_1\text{-C}_6$  alkenyl with one or two double bonds,
- (h)  $\text{-C}_1\text{-C}_6$  alkynyl with one or two triple bonds,
- (i)  $\text{-C}_1\text{-C}_6$  alkyl chain with one double bond and one triple bond,
- (j)  $\text{-R}_{1\text{-aryl}}$  where  $\text{R}_{1\text{-aryl}}$  is as defined above, or
- (k)  $\text{-R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-heteroaryl}}$  is as defined above,
- (8)  $\text{-CO-(C}_3\text{-C}_{12}\text{ alkyl)}$ ,
- (9)  $\text{-CO-(C}_3\text{-C}_6\text{ cycloalkyl)}$ ,
- (10)  $\text{-CO-R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-heteroaryl}}$  is as defined above,
- (11)  $\text{-CO-R}_{1\text{-heterocycle}}$  where  $\text{R}_{1\text{-heterocycle}}$  is as defined above,
- (12)  $\text{-CO-R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $\text{C}_1\text{-C}_3$  alkyl,
- (13)  $\text{-CO-O-R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  is:
  - (a)  $\text{C}_1\text{-C}_6$  alkyl, or
  - (b)  $\text{-(CH}_2\text{)}_{0-2}\text{-(R}_{1\text{-aryl}}\text{)}$  where  $\text{R}_{1\text{-aryl}}$  is as defined above,
- (14)  $\text{-SO}_2\text{-NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are as defined above,
- (15)  $\text{-SO-(C}_1\text{-C}_8\text{ alkyl)}$ ,
- (16)  $\text{-SO}_2\text{-(C}_3\text{-C}_{12}\text{ alkyl)}$ ,
- (17)  $\text{-NH-CO-O-R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  is as defined above,
- (18)  $\text{-NH-CO-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (19)  $\text{-N-CS-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,



(O) phthalazinyl,  
(P) imidazolyl,  
(Q) isoxazolyl,  
(R) pyrazolyl,  
(S) oxazolyl,  
(T) thiazolyl,  
(U) indolizinylyl,  
(V) indazolyl,  
(W) benzothiazolyl,  
(X) benzimidazolyl,  
(Y) benzofuranyl,  
(Z) furanyl,  
(AA) thienyl,  
(BB) pyrrolyl,  
(CC) oxadiazolyl,  
(DD) thiadiazolyl,  
(EE) triazolyl,  
(FF) tetrazolyl,  
(GG) 1, 4-benzodioxan  
(HH) purinyl,  
(II) oxazolopyridinyl,  
(JJ) imidazopyridinyl,  
(KK) isothiazolyl,  
(LL) naphthyridinyl,  
(MM) cinnolinyl,  
(NN) carbazolyl,  
(OO)  $\beta$ -carbolinyl,  
(PP) isochromanlyl,  
(QQ) chromanyl,  
(RR) furazanyl,  
(SS) tetrahydroisoquinoline,



(TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,
  - (c) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with 1, 2, or 3 -F, -Cl, -Br, or -I,
  - (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
  - (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
  - (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
  - (g) -C<sub>1</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(h)  $-C_1-C_6$  alkynyl with one or two triple bonds,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,  
or

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(8)  $-CO-(C_3-C_{12}$  alkyl),

(9)  $-CO-(C_3-C_6$  cycloalkyl),

(10)  $-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(11)  $-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,

(12)  $-CO-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3$  alkyl,

(13)  $-CO-O-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $C_1-C_6$  alkyl, or

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,

(14)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(15)  $-SO-(C_1-C_8$  alkyl),

(16)  $-SO_2-(C_3-C_{12}$  alkyl),

(17)  $-NH-CO-O-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(18)  $-NH-CO-N(C_1-C_3$  alkyl) $_2$ ,

(19)  $-N-CS-N(C_1-C_3$  alkyl) $_2$ ,

(20)  $-N(C_1-C_3 \text{ alkyl})-CO-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,

(25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,

(26)  $-O-(C_1-C_6 \text{ alkyl})$ ,

(27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ , or

(28)  $-S-(C_1-C_6 \text{ alkyl})$ ,

(C)  $-R_{N-aryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(D)  $-R_{N-aryl}-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,

(E)  $-R_{N-heteroaryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,

(F)  $-R_{N-heteroaryl}-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(G)  $-R_{N-aryl}-O-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(H)  $-R_{N-aryl}-S-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(I)  $-R_{N-heteroaryl}-O-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(J)  $-R_{N-heteroaryl}-S-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(K)  $-R_{N-aryl}-CO-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(L)  $-R_{N-aryl}-CO-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above,

(M)  $-R_{N-aryl}-SO_2-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(N)  $-R_{N-heteroaryl}-CO-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(O)  $-R_{N-heteroaryl}-SO_2-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(P)  $-R_{N-aryl}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N-aryl}$  is as defined above,

(Q)  $-R_{N-aryl}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N-aryl}$  is as defined above,

(R)  $-R_{N\text{-heteroaryl}}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or

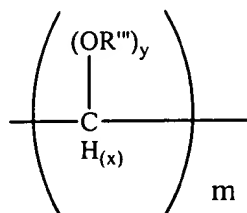
(S)  $-R_{N\text{-heteroaryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $A-X_N-$  where  $X_N$  is  $-\text{CO}-$ ,

wherein A is

(A)  $-T-E-(Q)_{m'}$ ,

(1) where  $-T$  is



where

- (a)  $x = 1$  when  $y = 1$  and  $x = 2$  when  $y = 0$ ,
- (b)  $m$  is 0, 1, 2 or 3,
- (c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and
- (d)  $R'''$  varies independently on each carbon and is H,  $(C_1-C_2)$  alkyl, phenyl, or phenyl $(C_1-C_3)$ alkyl;

(2)  $-E$  is

- (a)  $C_1-C_5$  alkyl, but only if  $m'$  does not equal 0,
- (b) methylthioxy $(C_2-C_4)$ alkyl,
- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -E(Q)<sub>m</sub> wherein E and -Q are as defined as above and m is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III)  $-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two:

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1\text{-C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1\text{-C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1\text{-C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  is the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1\text{-C}_5 \text{ alkyl})-\text{COOH}$ ,

(IV)  $-\text{CO}-(\text{C}_1\text{-C}_3 \text{ alkyl})-\text{O}-(\text{C}_1\text{-C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1\text{-C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1\text{-C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1\text{-C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,

- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,
- (V)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{S}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(VI) -CO-CH(-(CH<sub>2</sub>)<sub>0-2</sub>-O-R<sub>N-10</sub>)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>N-aryl</sub>/R<sub>N-heteroaryl</sub>) where R<sub>N-aryl</sub>

and R<sub>N-heteroaryl</sub> are as defined above, where R<sub>N-10</sub> is:

(A) -H,

(B) C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,

(E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,

(F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or

(G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above;

where B is -O-, -NH-, or -N(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

where R<sub>C</sub> is:

(I) -(C<sub>1</sub>-C<sub>10</sub>)alkyl-K<sub>1-3</sub> in which:

(A) the alkyl chain is unsubstituted or substituted with one -OH,

(B) the alkyl chain is unsubstituted or substituted with one C<sub>1</sub>-C<sub>6</sub> alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one -O-φ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 -F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C<sub>1</sub>-C<sub>3</sub> alkyl,

(3) C<sub>1</sub>-C<sub>3</sub> alkoxy,

(4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,

(5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,

(6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,

(7) amido

(8) C<sub>1</sub>-C<sub>6</sub> alkylamino



- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy, . . .
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,
- (B) -CO-OH,
- (C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),
- (D) -OH, or
- (E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(IV) -(CH<sub>2</sub>)<sub>2-6</sub>-OH,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are -H, C<sub>1</sub>-C<sub>4</sub> alkyl and  $\phi$ - and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub>,

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is:

- (A) pyridinyl,

- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) isoxazolyl,
- (Q) pyrazolyl,
- (R) indolizinyl,
- (S) indazolyl,
- (T) benzothiazolyl,
- (U) benzimidazolyl,
- (V) benzofuranyl,
- (W) furanyl,
- (X) thienyl,
- (Y) pyrrolyl,
- (Z) oxadiazolyl,
- (AA) thiadiazolyl,
- (BB) triazolyl,
- (CC) tetrazolyl,
- (DD) 1, 4-benzodioxan
- (EE) purinyl,
- (FF) oxazolopyridinyl,

- (GG) imidazopyridinyl,
- (HH) isothiazolyl,
- (II) naphthyridinyl,
- (JJ) cinnolinyl,
- (KK) carbazolyl,
- (LL)  $\beta$ -carbolinyl,
- (MM) isochromanyl,
- (NN) chromanyl,
- (OO) furazanyl,
- (PP) tetrahydroisoquinoline,
- (QQ) isoindolinyl,
- (RR) isobenzotetrahydrofuranyl,
- (SS) isobenzotetrahydrothienyl,
- (TT) isobenzothiophenyl,
- (UU) benzoxazolyl, or
- (VV) pyridopyridinyl,
- (VII)  $-(CH_2)_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{I-heterocycle}$ ,
- (VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:
  - (A) -H,
  - (B)  $-C_1-C_6$  alkyl,
  - (C)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above for  $R_{I-aryl}$ ,
  - (D)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
  - (E)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
  - (F)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
  - (G)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
  - (H)  $-(CH_2)_{1-4}-OH$ ,
  - (I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'-aryl}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$ ,  $-NH-$  or



$-\text{NHR}_{\text{C-5}}$  where  $\text{R}_{\text{C-5}}$  is  $\text{C}_1\text{-C}_6$  alkyl, and where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(J)  $-(\text{CH}_2)_{1-4}\text{-R}_{\text{C-4}}\text{-(CH}_2)_{1-4}\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-4}}$  and  $\text{R}_{\text{C-heteroaryl}}$  are as defined above, or

(K)  $-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above, . . .

and where  $\text{R}_{\text{C-3}}$  is:

(A)  $-\text{H}$ ,

(B)  $-\text{C}_1\text{-C}_6$  alkyl,

(C)  $-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(D)  $-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(E)  $-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(F)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(G)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

or

(H)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(IX)  $-\text{CH}(\phi)_2$ ,

(X)  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A)  $\text{C}_1\text{-C}_3$  alkyl,

(B)  $-\text{CF}_3$ ,

(C)  $-\text{F}$ ,  $\text{Cl}$ ,  $-\text{Br}$  and  $-\text{I}$ ,

(D)  $\text{C}_1\text{-C}_3$  alkoxy,

(E)  $-\text{OCF}_3$ ,

(F)  $-\text{NH}_2$ ,

(G)  $-\text{OH}$ , or

(H)  $-\text{C}\equiv\text{N}$ ,

(XI)  $-\text{CH}_2\text{-C}\equiv\text{CH}$ ;

(XII)  $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-5}}\text{-(CH}_2)_{0-1}\text{-}\phi$  where  $\text{R}_{\text{C-5}}$  is:

(A)  $-\text{OH}$ , or

- (B)-CH<sub>2</sub>-OH;  
 (XIII) -CH(-φ)-CO-O(C<sub>1</sub>-C<sub>3</sub> alkyl);  
 (XIV) -CH(-CH<sub>2</sub>-OH)-CH(-OH)-φ-NO<sub>2</sub>;  
 (XV) -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-OH;  
 (XVI) -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH(-O-CH<sub>2</sub>-CH<sub>3</sub>)<sub>2</sub>;  
 (XVII) -(C<sub>2</sub>-C<sub>8</sub>) alkynyl; or  
 (XVIII) -H; or a pharmaceutically acceptable salt thereof.

2. A method for inhibiting β-secretase activity according to 1  
 where R<sub>1</sub> is:

- (V) -(CH<sub>2</sub>)<sub>0-3</sub>-(R<sub>1</sub>-aryl), or  
 (VI) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1</sub>-heteroaryl)

where R<sub>N</sub> is:

(I) R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is:

- (A) -CO-, or  
 (B) -SO<sub>2</sub>-,

where R<sub>N-1</sub> is:

- (A) R<sub>N</sub>-aryl, or  
 (B) -R<sub>N</sub>-heteroaryl,  
 (VI) -CO-CH(-(CH<sub>2</sub>)<sub>0-2</sub>-O-R<sub>N-10</sub>)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>N</sub>-aryl/R<sub>N</sub>-heteroaryl)

where R<sub>C</sub> is:

- (I)-C<sub>1</sub>-C<sub>8</sub> alkyl,  
 (III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl,  
 (IV) -(CH<sub>2</sub>)<sub>0-3</sub>-OH,  
 (V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C</sub>-aryl,  
 (VI) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C</sub>-heteroaryl,  
 (VII) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C</sub>-heterocycle,  
 (VIII) -C(R<sub>C-1</sub>)(R<sub>C-2</sub>)-CO-NH-R<sub>C-3</sub>, or  
 (X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring  
 where heteroaryl is as defined above and phenyl and heteroaryl are  
 unsubstituted or substituted with one or two:

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl,

- (B)  $-\text{CF}_3$ ,
- (C)  $-\text{F}$ ,  $\text{Cl}$ ,  $-\text{Br}$  or  $-\text{I}$ ,
- (D)  $\text{C}_1$ - $\text{C}_3$  alkoxy, or
- (E)  $-\text{OCF}_3$ .

3. A method for inhibiting  $\beta$ -secretase activity according to claim 85 <sup>✓</sup> where  $\text{R}_1$  is:

- (V)  $-\text{CH}_2-(\text{R}_{1\text{-aryl}})$ , or
- (VI)  $-\text{CH}_2-(\text{R}_{1\text{-heteroaryl}})$ ;

where  $\text{R}_2$  is  $-\text{H}$ ;

where  $\text{R}_N$  is:

- (I)  $\text{R}_{\text{N-1}}-\text{X}_\text{N}$  where  $\text{X}_\text{N}$  is:
- (A)  $-\text{CO}-$ ,

where  $\text{R}_{\text{N-1}}$  is:

- (A)  $\text{R}_{\text{N-aryl}}$ , or
- (B)  $-\text{R}_{\text{N-heteroaryl}}$ ,

where  $\text{R}_\text{C}$  is:

- (III)  $-(\text{CH}_2)_{0-3}-(\text{C}_3-\text{C}_7)$  cycloalkyl,
- (V)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}$ ,
- (VI)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{C-heteroaryl}}$ ,
- (VII)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{C-heterocycle}}$ ,
- (VIII)  $-\text{C}(\text{R}_{\text{C-1}})(\text{R}_{\text{C-2}})-\text{CO}-\text{NH}-\text{R}_{\text{C-3}}$ , or
- (X)  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to a phenyl or heteroaryl ring.

4. A method for inhibiting  $\beta$ -secretase activity according to claim 3 <sup>✓</sup> where  $\text{R}_\text{C}$  is:

- (V)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}$ ,
- (VI)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{C-heteroaryl}}$ , or
- (X)  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to a phenyl or heteroaryl ring.

5. A method for inhibiting  $\beta$ -secretase activity according to claim 1 <sup>✓</sup> where  $\text{R}_1$  is:

$-\text{CH}_2-(\text{R}_{1\text{-aryl}})$  where  $\text{R}_{1\text{-aryl}}$  is phenyl.

6. A method for inhibiting  $\beta$ -secretase activity according to claim 5 <sup>✓</sup> where  $\text{R}_1$  is:

-CH<sub>2</sub>-(R<sub>1-aryl</sub>) where R<sub>1-aryl</sub> is phenyl substituted with two -F.

7. A method for inhibiting  $\beta$ -secretase activity according to claim 6 where phenyl is substituted with two -F in the 3- and 5- positions giving 3,5-difluorophenyl.

8. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>2</sub> is:

(I) -H,

(II) C<sub>1</sub>-C<sub>6</sub> alkyl, or

(III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub>.

9. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>2</sub> is:

(II) C<sub>1</sub>-C<sub>6</sub> alkyl, or

(III) benzyl.

10. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>N</sub> is

R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl substituted with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where the substitution on phenyl is 1,3-.

11. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>N-2</sub> and R<sub>N-3</sub> are the same and are C<sub>3</sub> alkyl.

12. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>N</sub> is

R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is -CO-, where R<sub>N-1</sub> is R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl substituted with one C<sub>1</sub> alkyl and with one -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where the substitution on the phenyl is 1,3,5-.

13. A method for inhibiting  $\beta$ -secretase activity according to claim 12 where R<sub>N-2</sub> and R<sub>N-3</sub> are the same and are C<sub>3</sub> alkyl.

14. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where R<sub>N</sub> is

$R_{N-1}-X_N-$  where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is substituted with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$ .

15. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_{N-2}$  and  $R_{N-3}$  are the same and are  $-\text{C}_3$  alkyl.

16. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_N$  is:

$\text{A}-X_N-$  where  $X_N$  is  $-\text{CO}-$ , where A is:

(C)  $\text{C}_{10}\text{H}_7-\text{CH}(\text{OH})-$ , or

(D) t-butoxy.

17. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_C$  is:

(V)  $-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C\text{-aryl}}$ ,

(VI)  $-(\text{CH}_2)_{0-4}-\text{R}_{C\text{-heteroaryl}}$ ,

(VII)  $-(\text{CH}_2)_{0-4}-\text{R}_{C\text{-heterocycle}}$ ,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one or two:

(A)  $\text{C}_1-\text{C}_3$  alkyl,

(B)  $-\text{CF}_3$ ,

(C)  $-\text{F}$ ,  $\text{Cl}$ ,  $-\text{Br}$  or  $-\text{I}$ ,

(D)  $\text{C}_1-\text{C}_3$  alkoxy,

(E)  $-\text{OCF}_3$ , or

(XVIII)  $-\text{H}$ .

18. A method for inhibiting  $\beta$ -secretase activity according to claim 17 where  $R_C$  is:

(V)  $-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C\text{-aryl}}$  where  $\text{R}_{C\text{-aryl}}$  is phenyl.

19. A method for inhibiting  $\beta$ -secretase activity according to claim 18 where phenyl substituted in the 3-position or 3,5-positions.

20. A method for inhibiting  $\beta$ -secretase activity according to claim 17 where  $R_C$  is:



(VI)  $-\text{CH}_2-\text{R}_\text{C}$ -heteroaryl,

21. A method for inhibiting  $\beta$ -secretase activity according to claim 17 where  $\text{R}_\text{C}$  is:

(VII)  $-\text{CH}_2-\text{R}_\text{C}$ -heterocycle.

22. A method for inhibiting  $\beta$ -secretase activity according to claim 17 where  $\text{R}_\text{C}$  is:

(X) -cyclohexyl ring fused to a phenyl ring.

23. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $\text{R}_\text{C}$  is:

(I)  $-(\text{C}_1-\text{C}_{10})\text{alkyl}-\text{K}_{1-3}$  where each K is:

(1) H,

(11) carboxyl,

(16) amino unsubstituted or substituted with  $\text{C}_1-\text{C}_6$  alkyl; or

(18) carboxyl methyl ester;

(II)  $-(\text{CH}_2)_{0-3}-\text{J}-[\text{K}]_{1-3}$ , where J is:

(A) a 5 to 7 atom monocyclic aryl group, or

(B) a 5 to 10 atom multicyclic cycloalkyl group,

and each K is:

(1) H,

(3)  $\text{C}_1-\text{C}_3$  alkoxy, or

(11) carboxyl,

(III)  $-(\text{CH}_2)_{0-3}-(\text{C}_3-\text{C}_7)$  cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three:

(B)  $-\text{CO}-\text{OH}$ ,

(C)  $-\text{CO}-\text{O}-(\text{C}_1-\text{C}_4 \text{ alkyl})$ , or

(E)  $\text{C}_1-\text{C}_6$  alkoxy,

(IV)  $-(\text{CH}_2)_{2-6}-\text{OH}$ ,

(V)  $-(\text{CH}_2)_{0-4}-\text{R}_\text{C}$ -aryl,

(VI)  $-(\text{CH}_2)_{0-4}-\text{R}_\text{C}$ -heteroaryl,

(VII)  $-(\text{CH}_2)_{0-4}-\text{R}_\text{C}$ -heterocycle, or

(XVIII)  $-(\text{C}_2-\text{C}_8)$  alkynyl.

24. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_C$  is:

- (I)  $-(C_1-C_{10})alkyl-K$  where K is H, carboxyl, carboxyl methyl ester, amino unsubstituted or substituted with  $C_1-C_6$  alkyl,
- (II) a benzyl or phenylpropyl group substituted with a carboxyl group,
- (III)  $-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl where cycloalkyl is cyclohexyl, cyclohexyl substituted with 1 or 2 carboxyl groups, or cyclohexyl substituted with 1 or 2 alkoxy groups,
- (V)  $-(CH_2)_{0-4}$ -phenyl substituted or unsubstituted with F,
- (VI)  $-(CH_2)_{0-4}$ -heteroaryl, or
- (VII) selected from  $-(CH_2)_{0-4}$ -morpholinyl and  $-(CH_2)_{0-4}$ -tetrahydrofuryl.

25. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_C$  is:

- (I)  $C_5H_{10}-K$  or  $C_7H_{14}-K$  where K is carboxyl or carboxyl methyl ester,
- (II) a benzyl or phenylpropyl group substituted with a carboxyl group at the 5-position, or
- (III) a cyclohexyl ring substituted at the 3- and 5- positions or at the 4-position with a carboxyl group.

26. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where  $R_1$  is:

- (I)  $C_1-C_5$  alkyl,
  - (II)  $-(CH_2)_{1-2}-S-CH_3$ ,
  - (IV)  $C_1-C_5$  alkenyl,
  - (V)  $-(CH_2)_{0-3}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above, and
  - (VI)  $-(CH_2)_{0-3}-(R_{1-heteroaryl})$  where  $R_{1-heteroaryl}$  is as defined above,
- wherein any of the above are unsubstituted or substituted with up to two  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, or  $-CF_3$ ;

where  $R_2$  is:

- (I) -H,
- (II)  $C_1-C_6$  alkyl, or

(III)  $-(CH_2)_{0-3}-R_{2-1}$  where  $R_{2-1}$  is  $(C_3-C_6)$ cycloalkyl,  $R_{1-aryl}$  or  $R_{1-heteroaryl}$   
 where  $R_{1-aryl}$  is a 5 or 6-membered aryl group and  $R_{1-heteroaryl}$  is as  
 defined above;

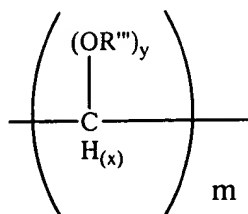
where  $R_N$  is:

(II)  $A-X_N-$  where  $X_N$  is  $-CO-$ ,

wherein A is

(A)  $-T-E-(Q)_{m'}$ ,

(1) where  $-T$  is



where

- (a)  $x = 1$  when  $y = 1$  and  $x = 2$  when  $y = 0$ ,
- (b)  $m$  is 0, 1, 2 or 3,
- (c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and
- (d)  $R'''$  varies independently on each carbon and is H,  $(C_1-C_2)$  alkyl, phenyl, or phenyl $(C_1-C_3)$ alkyl;

(2)  $-E$  is

- (a)  $C_1-C_5$  alkyl, but only if  $m'$  does not equal 0,
- (b) methylthioxy $(C_2-C_4)$ alkyl,
- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,

- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -E(Q)<sub>m''</sub> wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

where R<sub>C</sub> is:

(I) -(C<sub>1</sub>-C<sub>10</sub>)alkyl-K<sub>1-3</sub>

(E) the alkyl chain optionally contains a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,  
(F) each K is:

- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido,
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl,
- (11) carboxyl,
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is:

- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido,
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl,

- (11) carboxyl,
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom monocyclic heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

and

where B is O or NH.

27. A method for inhibiting  $\beta$ -secretase activity according to claim 1 where the pharmaceutically acceptable salt is a salt of hydrochloric, hydrobromic, hydroiodic, nitric, sulfuric, phosphoric, citric, methanesulfonic, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>n</sub>-COOH where n is 0 thru 4, HOOC-(CH<sub>2</sub>)<sub>n</sub>-COOH where n is as defined above, HOOC-CH=CH-COOH and  $\phi$ -COOH acid or triethanolamine, N-methylglucamine, diethanolamine, ethanolamine, tris(hydroxymethyl)aminomethane (TRIS), ammonia, or carbonate, bicarbonate, phosphonate, or hydroxide salts of an alkali or alkaline earth metal.

28. A method for inhibiting  $\beta$ -secretase activity according to claim 1 wherein said compound is:

N-[(1*S*, 2*S*, 4*R*)-1-(3,5-Difluorobenzyl)-4-(*syn*, *syn*)-(3,5-dimethoxycyclohexylcarbamoyl)-2-hydroxyhexyl]-*N,N*-dipropylisophthalamide,

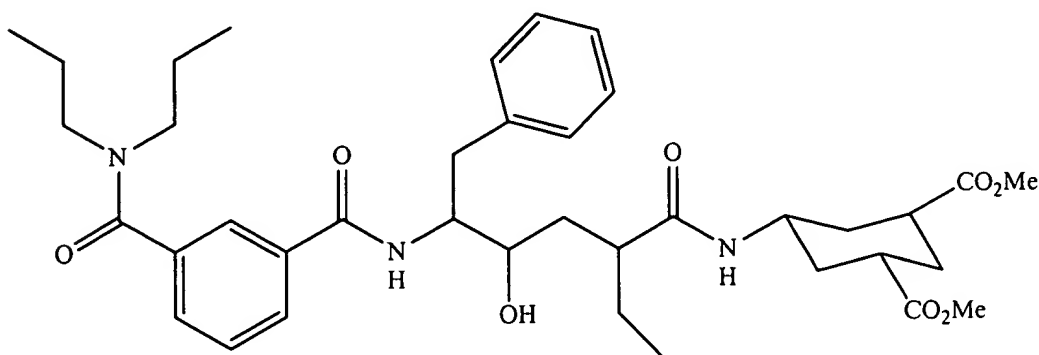
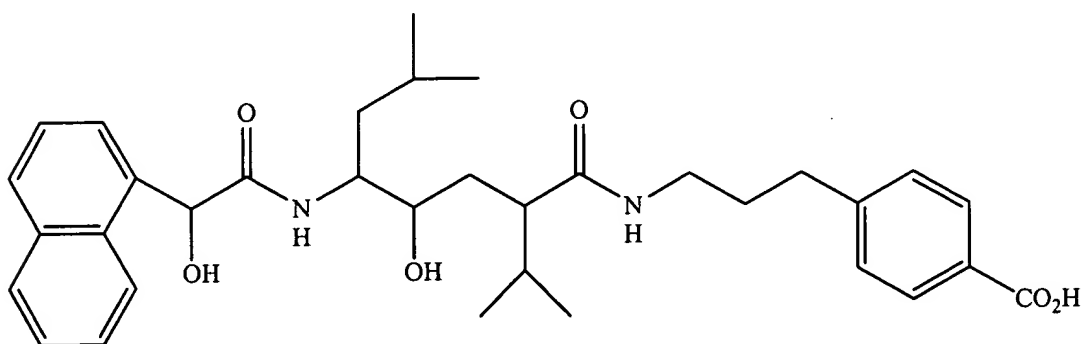
6-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-hexanoic acid,  
 5-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-pentanoic acid,  
 4-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-butyric acid,  
 3-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-propionic acid,  
 8-[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-octanoic acid,  
 8-[6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-octanoic acid methyl ester,  
*N*-[4-(*R*)-Butylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-isobutylcarbamoyl-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[4-(*R*)-Benzylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[4-(*R*)-(Cyclohexylmethyl-carbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(piperidine-1-carbonyl)-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(2-dimethylamino-ethylcarbamoyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[4-(*R*)-(Butyl-methyl-carbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(3-hydroxy-propylcarbamoyl)-hexyl]-*N,N*-dipropyl-isophthalamide,  
 4-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester,

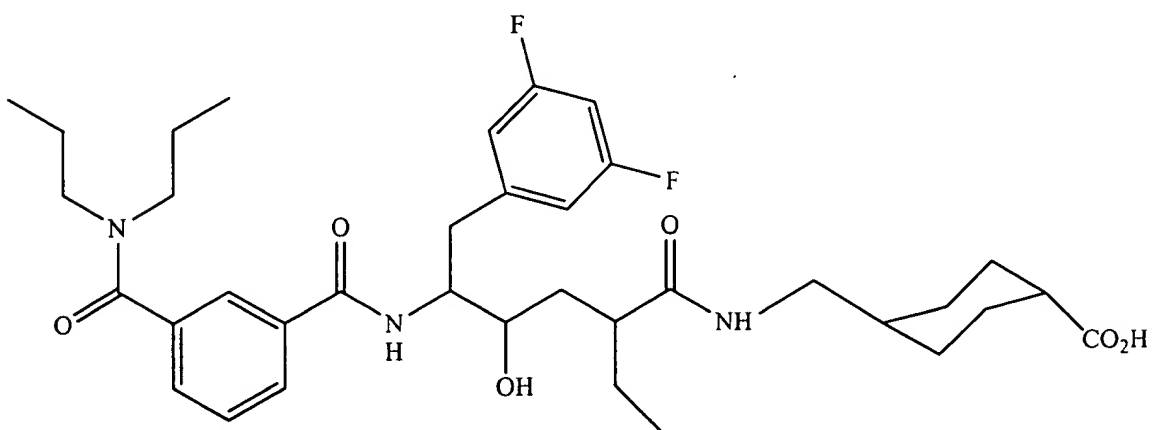
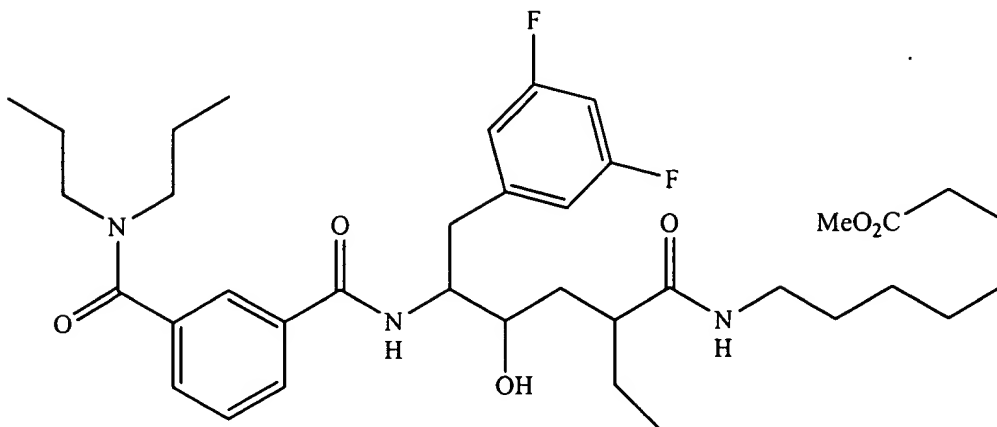
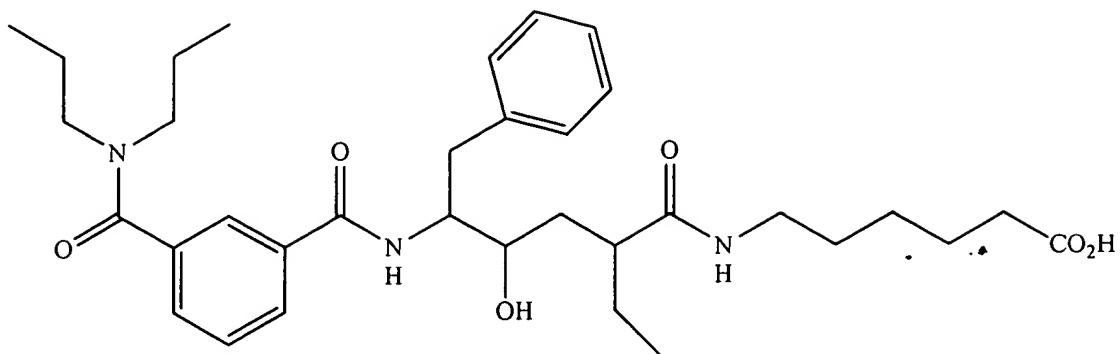
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(3-dimethylamino-propylcarbamoyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-methyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-propyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxyl-2-(*R*)-isobutyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([2-(*R*)-Benzyl-6-(3,5-difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid,  
 4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(2-morpholin-4-yl-ethylcarbamoyl)-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-isobutylcarbamoyl-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[4-(*R*)-(2-Diethylamino-ethylcarbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-[(tetrahydro-furan-2-ylmethyl)-carbamoyl]-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[4-(*R*)-(Adamantan-2-ylcarbamoyl)-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-methyl-5-morpholin-4-yl-5-oxo-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,

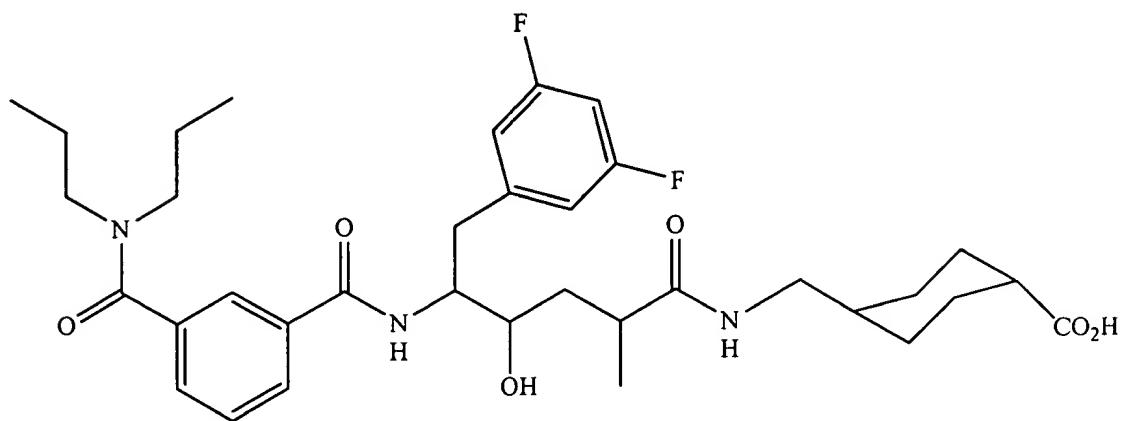
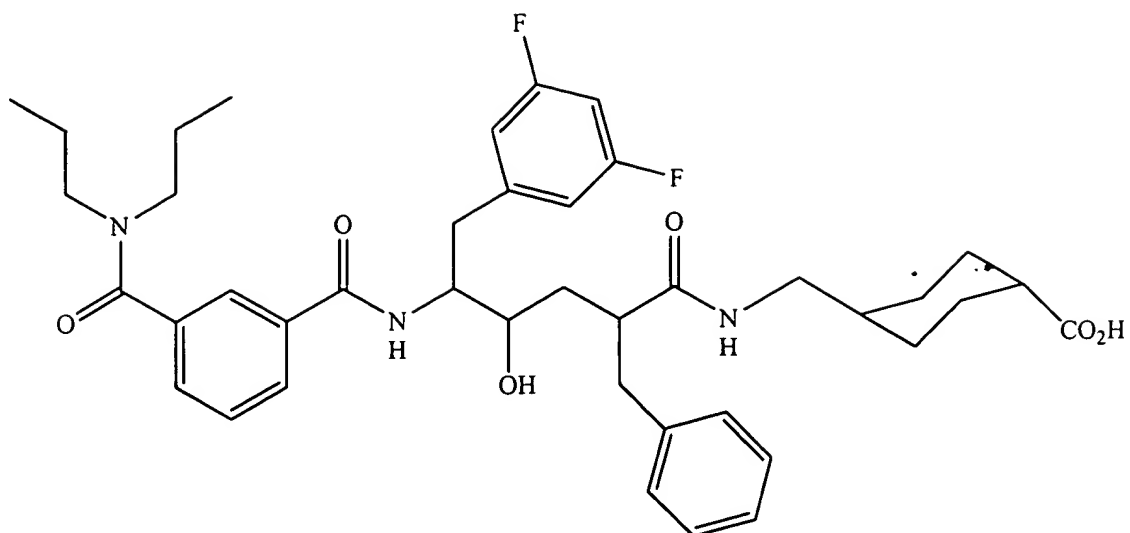


*N*-[4-(*R*)-Benzylcarbamoyl-1-(*S*)-(3,5-difluoro-benzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-(4-fluoro-benzylcarbamoyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide;  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-phenethylcarbamoyl-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide,  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-4-(*R*)-[(furan-2-ylmethyl)-carbamoyl]-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide, or  
*N*-[1-(*S*)-(3,5-Difluoro-benzyl)-2-(*S*)-hydroxy-4-(*R*)-(prop-2-ynylcarbamoyl)-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide.

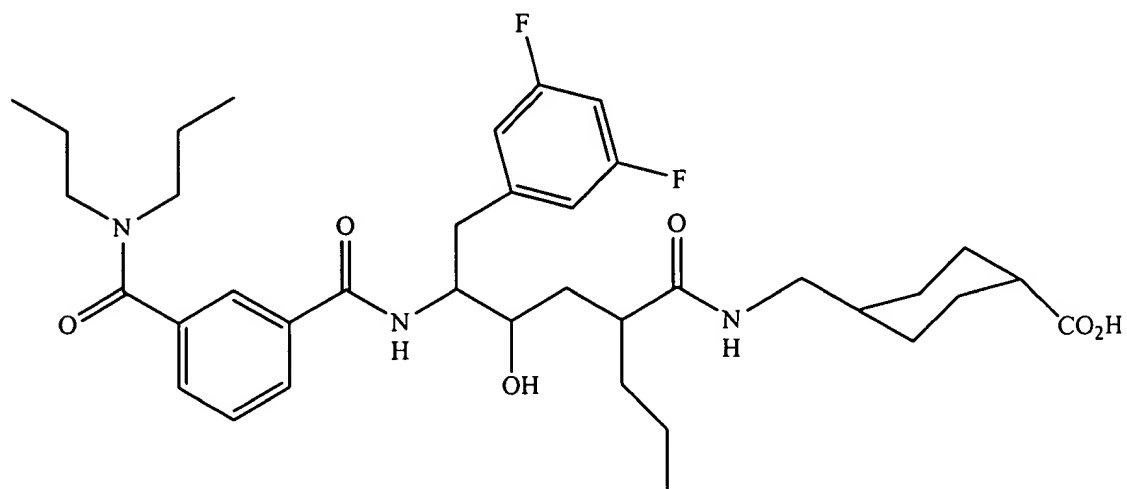
29. A method for inhibiting  $\beta$ -secretase activity according to claim 1 wherein said compound is:







OR



30. The method of claim 1, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 0.1nM to about 200μM.

31. The method of claim 30, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 10nM to about 100μM.

32. The method of claim 31, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 100nM to about 50μM.

33. The method of claim 32, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 1μM to about 10μM.

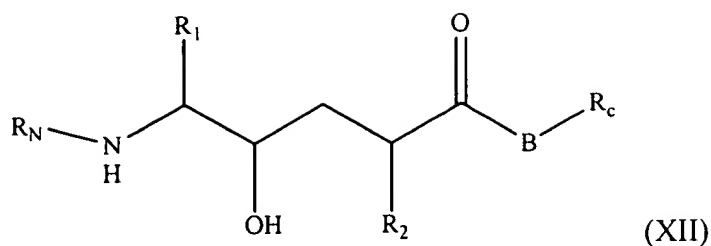
34. The method of claim 1, wherein said β-secretase is exposed to said compound *in vitro*.

35. The method of claim 1, wherein said β-secretase is exposed to said compound in a cell.

36. The method of claim 35, wherein said cell is in an animal.

37. The method of claim 36, wherein said animal is a human.

38. A method for inhibiting amyloid precursor protein (APP) cleavage in a reaction mixture at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a hydroxyethylene compound of the formula



where  $R_1$  is:

- (I)  $C_1-C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-NH_2$ ,  $-C\equiv N$ ,  $-CF_3$ , or  $-N_3$ ,
- (II)  $-(CH_2)_{1-2}-S-CH_3$ ,
- (III)  $-CH_2-CH_2-S-CH_3$ ,
- (IV)  $-CH_2-(C_2-C_6 \text{ alkenyl})$  unsubstituted or substituted by one  $-F$ ,
- (V)  $-(CH_2)_{0-3}-(R_{1-aryl})$  where  $R_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:
  - (A)  $C_1-C_3$  alkyl,
  - (B)  $-CF_3$ ,
  - (C)  $-F$ ,  $Cl$ ,  $-Br$  and  $-I$ ,
  - (D)  $C_1-C_3$  alkoxy,
  - (E)  $-O-CF_3$ ,
  - (F)  $-NH_2$ ,
  - (G)  $-OH$ , or
  - (H)  $-C\equiv N$ ,
- (VI)  $-(CH_2)_{n_1}-(R_{1-heteroaryl})$  where  $n_1$  is 0, 1, 2, or 3 and  $R_{1-heteroaryl}$  is:
  - (A) pyridinyl,
  - (B) pyrimidinyl,
  - (C) quinolinyl,
  - (D) indenyl,
  - (E) indanyl,
  - (F) benzothiophenyl,

(G) indolyl,  
(H) indolinyl,  
(I) pyridazinyl,  
(J) pyrazinyl,  
(K) isoindolyl,  
(L) isoquinolyl,  
(M) quinazolinyl,  
(N) quinoxalinyl,  
(O) phthalazinyl,  
(P) imidazolyl,  
(Q) isoxazolyl,  
(R) pyrazolyl,  
(S) oxazolyl,  
(T) thiazolyl,  
(U) indolizinyll,  
(V) indazolyl,  
(W) benzothiazolyl,  
(X) benzimidazolyl,  
(Y) benzofuranyl,  
(Z) furanyl,  
(AA) thienyl,  
(BB) pyrrolyl,  
(CC) oxadiazolyl,  
(DD) thiadiazolyl,  
(EE) triazolyl,  
(FF) tetrazolyl,  
(GG) 1, 4-benzodioxan  
(HH) purinyl,  
(II) oxazolopyridinyl,  
(JJ) imidazopyridinyl,  
(KK) isothiazolyl,

(LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1$ - $C_3$  alkoxy,
- (5)  $-O-CF_3$ ,
- (6)  $-NH_2$ ,
- (7)  $-OH$ , or
- (8)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $-(CH_2)_{n_1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and

$R_{1\text{-heterocycle}}$  is:

(A) morpholinyl,

- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranlyl, or
- (L) tetrahydrothiophenyl,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2)  $C_1\text{-}C_3$  alkyl,
- (3)  $-CF_3$ ,
- (4) -F, Cl, -Br and -I,
- (5)  $C_1\text{-}C_3$  alkoxy,
- (6)  $-O-CF_3$ ,
- (7)  $-NH_2$ ,
- (8) -OH, or
- (9)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $R_2$  is:

- (I) -H,
- (II)  $C_1\text{-}C_6$  alkyl, or
- (III)  $-(CH_2)_{0-4}\text{-}R_{2-1}$  where  $R_{2-1}$  is  $(C_3\text{-}C_6)\text{cycloalkyl}$ ,  $R_{1\text{-aryl}}$  or  $R_{1\text{-heteroaryl}}$   
where  $R_{1\text{-aryl}}$  and  $R_{1\text{-heteroaryl}}$  are as defined above,



where  $R_N$  is:

(I)  $R_{N-1}-X_N$ - where  $X_N$  is:

- (A)  $-\text{CO}-$ ,
- (B)  $-\text{SO}_2-$ ,
- (C)  $-(\text{CR}'\text{R}'')_{1-6}$  where  $\text{R}'$  and  $\text{R}''$  are the same or different and are  $-\text{H}$  or  $\text{C}_1-\text{C}_4$  alkyl,
- (D)  $-\text{CO}-(\text{CR}'\text{R}'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'\text{R}''-$  and where  $\text{R}'$  and  $\text{R}''$  are as defined above,
- (E) a single bond;

where  $R_{N-1}$  is:

(A)  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1)  $\text{C}_1-\text{C}_6$  alkyl,
- (2)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,
- (3)  $-\text{OH}$ ,
- (4)  $-\text{NO}_2$ ,
- (5)  $-\text{CO}-\text{OH}$ ,
- (6)  $-\text{C}\equiv\text{N}$ ,
- (7)  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where  $\text{R}_{N-2}$  and  $\text{R}_{N-3}$  are the same or different and are:

- (a)  $-\text{H}$ ,
- (b)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one
  - (i)  $-\text{OH}$ , or
  - (ii)  $-\text{NH}_2$ ,
- (c)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one to three  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,
- (d)  $-\text{C}_3-\text{C}_7$  cycloalkyl,
- (e)  $-(\text{C}_1-\text{C}_2 \text{ alkyl})-(\text{C}_3-\text{C}_7 \text{ cycloalkyl})$ ,

- (f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,
- (g)  $-C_1-C_6 \text{ alkenyl}$  with one or two double bonds,
- (h)  $-C_1-C_6 \text{ alkynyl}$  with one or two triple bonds,
- (i)  $-C_1-C_6 \text{ alkyl chain}$  with one double bond and one triple bond,
- (j)  $-R_{1\text{-aryl}}$  where  $R_{1\text{-aryl}}$  is as defined above, or
- (k)  $-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,
- (8)  $-\text{CO}-(C_3-C_{12} \text{ alkyl})$ ,
- (9)  $-\text{CO}-(C_3-C_6 \text{ cycloalkyl})$ ,
- (10)  $-\text{CO}-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,
- (11)  $-\text{CO}-R_{1\text{-heterocycle}}$  where  $R_{1\text{-heterocycle}}$  is as defined above,
- (12)  $-\text{CO}-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3 \text{ alkyl}$ ,
- (13)  $-\text{CO}-O-R_{N-5}$  where  $R_{N-5}$  is:
  - (a)  $C_1-C_6 \text{ alkyl}$ , or
  - (b)  $-(CH_2)_{0-2}-(R_{1\text{-aryl}})$  where  $R_{1\text{-aryl}}$  is as defined above,
- (14)  $-\text{SO}_2-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,
- (15)  $-\text{SO}-(C_1-C_8 \text{ alkyl})$ ,
- (16)  $-\text{SO}_2-(C_3-C_{12} \text{ alkyl})$ ,
- (17)  $-\text{NH}-\text{CO}-O-R_{N-5}$  where  $R_{N-5}$  is as defined above,
- (18)  $-\text{NH}-\text{CO}-N(C_1-C_3 \text{ alkyl})_2$ ,
- (19)  $-\text{N}-\text{CS}-N(C_1-C_3 \text{ alkyl})_2$ ,
- (20)  $-\text{N}(C_1-C_3 \text{ alkyl})-\text{CO}-R_{N-5}$  where  $R_{N-5}$  is as defined above,
- (21)  $-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,
- (22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

- (23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,  
 (25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,  
 (26)  $-O-(C_1-C_6 \text{ alkyl})$ ,  
 (27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ ,  
 (28)  $-S-(C_1-C_6 \text{ alkyl})$ ,  
 (29)  $C_1-C_6 \text{ alkyl}$  unsubstituted or substituted with 1, 2, 3, 4,  
 or 5  $-F$ ,  
 (30)  $-O-(C_1-C_6 \text{ alkyl}$  unsubstituted or substituted with 1, 2,  
 3, 4, or 5  $-F$ , or  
 (31)  $-O-\phi$ ,

(B)  $-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is:

- (A) pyridinyl,  
 (B) pyrimidinyl,  
 (C) quinolinyl,  
 (D) indenyl,  
 (E) indanyl,  
 (F) benzothiophenyl,  
 (G) indolyl,  
 (H) indolinyl,  
 (I) pyridazinyl,  
 (J) pyrazinyl,  
 (K) isoindolyl,  
 (L) isoquinolyl,  
 (M) quinazolinyl,  
 (N) quinoxalinyl,  
 (O) phthalazinyl,  
 (P) imidazolyl,  
 (Q) isoxazolyl,  
 (R) pyrazolyl,  
 (S) oxazolyl,

(T) thiazolyl,  
 (U) indolizinyl,  
 (V) indazolyl,  
 (W) benzothiazolyl,  
 (X) benzimidazolyl,  
 (Y) benzofuranyl,  
 (Z) furanyl,  
 (AA) thienyl,  
 (BB) pyrrolyl,  
 (CC) oxadiazolyl,  
 (DD) thiadiazolyl,  
 (EE) triazolyl,  
 (FF) tetrazolyl,  
 (GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (3)  $-OH$ ,
- (4)  $-NO_2$ ,
- (5)  $-CO-OH$ ,
- (6)  $-C\equiv N$ ,
- (7)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are:
  - (a)  $-H$ ,
  - (b)  $-C_1\text{-}C_6$  alkyl unsubstituted or substituted with one
    - (i)  $-OH$ , or
    - (ii)  $-NH_2$ ,
  - (c)  $-C_1\text{-}C_6$  alkyl unsubstituted or substituted with 1, 2, or 3  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
  - (d)  $-C_3\text{-}C_7$  cycloalkyl,
  - (e)  $-(C_1\text{-}C_2\text{ alkyl})\text{-}(C_3\text{-}C_7\text{ cycloalkyl})$ ,
  - (f)  $-(C_1\text{-}C_6\text{ alkyl})\text{-}O\text{-}(C_1\text{-}C_3\text{ alkyl})$ ,
  - (g)  $-C_1\text{-}C_6$  alkenyl with one or two double bonds,
  - (h)  $-C_1\text{-}C_6$  alkynyl with one or two triple bonds,
  - (i)  $-C_1\text{-}C_6$  alkyl chain with one double bond and one triple bond,
  - (j)  $-R_{1\text{-aryl}}$  where  $R_{1\text{-aryl}}$  is as defined above,  
or

(k)  $-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,

(8)  $-\text{CO}-(\text{C}_3\text{-C}_{12} \text{ alkyl})$ ,

(9)  $-\text{CO}-(\text{C}_3\text{-C}_6 \text{ cycloalkyl})$ ,

(10)  $-\text{CO}-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,

(11)  $-\text{CO}-R_{1\text{-heterocycle}}$  where  $R_{1\text{-heterocycle}}$  is as defined above,

(12)  $-\text{CO}-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $\text{C}_1\text{-C}_3$  alkyl,

(13)  $-\text{CO}-\text{O}-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $\text{C}_1\text{-C}_6$  alkyl, or

(b)  $-(\text{CH}_2)_{0-2}-(R_{1\text{-aryl}})$  where  $R_{1\text{-aryl}}$  is as defined above,

(14)  $-\text{SO}_2-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(15)  $-\text{SO}-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,

(16)  $-\text{SO}_2-(\text{C}_3\text{-C}_{12} \text{ alkyl})$ ,

(17)  $-\text{NH}-\text{CO}-\text{O}-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(18)  $-\text{NH}-\text{CO}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(19)  $-\text{N}-\text{CS}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(20)  $-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})-\text{CO}-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(21)  $-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,

(24)  $-\text{O}-\text{CO}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,

(26)  $-O-(C_1-C_6 \text{ alkyl})$ ,

(27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ , or

(28)  $-S-(C_1-C_6 \text{ alkyl})$ ,

(C)  $-R_{N\text{-aryl}}-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above, •

(D)  $-R_{N\text{-aryl}}-R_{N\text{-heteroaryl}}$  where  $-R_{N\text{-aryl}}$  and  $-R_{N\text{-heteroaryl}}$  are as defined above,

(E)  $-R_{N\text{-heteroaryl}}-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  and  $-R_{N\text{-heteroaryl}}$  are as defined above,

(F)  $-R_{N\text{-heteroaryl}}-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(G)  $-R_{N\text{-aryl}}-O-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,

(H)  $-R_{N\text{-aryl}}-S-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,

(I)  $-R_{N\text{-heteroaryl}}-O-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(J)  $-R_{N\text{-heteroaryl}}-S-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(K)  $-R_{N\text{-aryl}}-CO-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,

(L)  $-R_{N\text{-aryl}}-CO-R_{N\text{-heteroaryl}}$  where  $-R_{N\text{-aryl}}$  and  $R_{N\text{-heteroaryl}}$  are as defined above,

(M)  $-R_{N\text{-aryl}}-SO_2-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,

(N)  $-R_{N\text{-heteroaryl}}-CO-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(O)  $-R_{N\text{-heteroaryl}}-SO_2-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(P)  $-R_{N\text{-aryl}}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,

(Q)  $-R_{N\text{-aryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,

(R)  $-R_{N\text{-heteroaryl}}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or

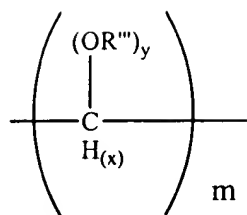
(S)  $-R_{N\text{-heteroaryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $A-X_N-$  where  $X_N$  is  $-CO-$ ,

wherein A is

(A) -T-E-(Q)<sub>m'</sub>,

(1) where -T is



where

- (a) x = 1 when y = 1 and x = 2 when y = 0,
- (b) m is 0, 1, 2 or 3,
- (c) the values of x and y vary independently on each carbon when m is 2 and 3, and
- (d) R''' varies independently on each carbon and is H, (C<sub>1</sub>-C<sub>2</sub>) alkyl, phenyl, or phenyl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

(2) -E is

- (a) C<sub>1</sub>-C<sub>5</sub> alkyl, but only if m' does not equal 0,
- (b) methylthioxy(C<sub>2</sub>-C<sub>4</sub>)alkyl,
- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,



- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
  - (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
  - (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
  - (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
  - (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
  - (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
  - (h) phenylamino,
  - (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
  - (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
  - (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
  - (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
  - (m) heterocyclacyl,
  - (n) heteroarylacyl, or
  - (o) hydroxyl;
- (4) m' is 0, 1, 2 or 3;

- (B) -E(Q)<sub>m</sub> wherein E and -Q are as defined as above and m is 0, 1, 2, or 3;
- (C) -T-E wherein -E and -Q are as defined as above; or
- (D) -E wherein -E is as defined as above;

(III) -CO-(C<sub>1</sub>-C<sub>6</sub> alkyl) where alkyl is unsubstituted or substituted with one or two:

- (A) -OH,
- (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
- (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,

- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  is the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,
- (IV)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or  
 (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,  
 (V)  $-CO-(C_1-C_3 \text{ alkyl})-S-(C_1-C_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
- (A)  $-OH$ ,  
 (B)  $-C_1-C_6 \text{ alkoxy}$ ,  
 (C)  $-C_1-C_6 \text{ thioalkoxy}$ ,  
 (D)  $-CO-O-R_{N-8}$  where  $R_{N-8}$  is  $-H$ ,  $C_1-C_6 \text{ alkyl}$  or  $-\phi$ ,  
 (E)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (F)  $-CO-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (G)  $-SO_2-(C_1-C_8 \text{ alkyl})$ ,  
 (H)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (I)  $-NH-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (J)  $-NH-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,  
 (K)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or  
 (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,  
 (VI)  $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-R_{N-aryl}/R_{N-heteroaryl}$  where  $R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above, where  $R_{N-10}$  is:
- (A)  $-H$ ,  
 (B)  $C_1-C_6 \text{ alkyl}$ ,  
 (C)  $C_3-C_7 \text{ cycloalkyl}$ ,

- (D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,  
 (E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,  
 (F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or  
 (G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above;

where B is -O-, -NH-, or -N(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

where R<sub>C</sub> is:

(I) -(C<sub>1</sub>-C<sub>10</sub>)alkyl-K<sub>1-3</sub> in which:

- (A) the alkyl chain is unsubstituted or substituted with one -OH,  
 (B) the alkyl chain is unsubstituted or substituted with one C<sub>1</sub>-C<sub>6</sub>  
 alkoxy unsubstituted or substituted with 1-5 -F,  
 (C) the alkyl chain is unsubstituted or substituted with one -O-φ,  
 (D) the alkyl chain is unsubstituted or substituted with 1-5 -F,  
 (E) the alkyl chain is unsubstituted or substituted with a  
 combination of up to three atoms of oxygen and sulfur each  
 such atom replacing one carbon,  
 (F) each K is:

- (1) H,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(D) -OH, or

(E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(IV) -(CH<sub>2</sub>)<sub>2-6</sub>-OH,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are -H, C<sub>1</sub>-C<sub>4</sub> alkyl and  $\phi$ - and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub>,

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

Q. Did you find any other evidence of the defendant's presence at the scene?

(MM) isochromanyl,  
 (NN) chromanyl,  
 (OO) furazanyl,  
 (PP) tetrahydroisoquinoline,  
 (QQ) isoindolinyl,  
 (RR) isobenzotetrahydrofuranyl,  
 (SS) isobenzotetrahydrothienyl,  
 (TT) isobenzothiophenyl,  
 (UU) benzoxazolyl, or  
 (VV) pyridopyridinyl,

(VII)  $-(CH_2)_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-heterocycle}$ ,

(VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:

- (A) -H,
- (B)  $-C_1-C_6$  alkyl,
- (C)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above for  $R_{1-aryl}$ ,
- (D)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (E)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (F)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (G)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (H)  $(CH_2)_{1-4}-OH$ ,
- (I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'-aryl}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$ ,  $-NH-$  or  $-NHR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'-aryl}$  is as defined above,
- (J)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C-heteroaryl}$  where  $R_{C-4}$  and  $R_{C-heteroaryl}$  are as defined above, or
- (K)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,

and where  $R_{C-3}$  is:

- (A) -H,





39. The method of claim 38, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype,; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

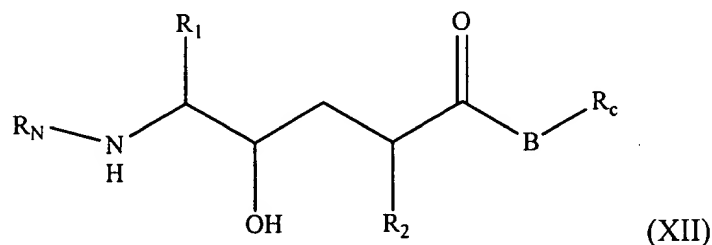
40. The method of claim 38, wherein said reaction mixture is exposed *in vitro*.

41. The method of claim 38, wherein said reaction mixture is exposed in a cell.

42. The method of claim 41, wherein said cell is in an animal.

43. The method of claim 42, wherein said animal is a human.

44. A method for inhibiting production of amyloid beta peptide ( $A\beta$ ) in a cell, comprising administering to said cell an effective inhibitory amount of a hydroxyethylene compound of the formula



where  $\text{R}_1$  is:

(I)  $\text{C}_1-\text{C}_6$  alkyl, unsubstituted or substituted with one, two or three  $\text{C}_1-\text{C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, - $\text{NH}_2$ , -C $\equiv$ N, - $\text{CF}_3$ , or - $\text{N}_3$ ,

(II)  $-(\text{CH}_2)_{1-2}-\text{S}-\text{CH}_3$ ,

(III)  $-\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_3$ ,

(IV)  $-\text{CH}_2-(\text{C}_2-\text{C}_6 \text{ alkenyl})$  unsubstituted or substituted by one -F,

(V)  $-(\text{CH}_2)_{0-3}-(\text{R}_{1-\text{aryl}})$  where  $\text{R}_{1-\text{aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or

substituted on the aryl ring with one or two of the following substituents which can be the same or different:

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (B) -CF<sub>3</sub>,
- (C) -F, Cl, -Br and -I,
- (D) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (E) -O-CF<sub>3</sub>,
- (F) -NH<sub>2</sub>,
- (G) -OH, or
- (H) -C≡N,

(VI) -(CH<sub>2</sub>)<sub>n<sub>1</sub></sub>-(R<sub>1</sub>-heteroaryl) where n<sub>1</sub> is 0, 1, 2, or 3 and R<sub>1</sub>-heteroaryl is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,

(U) indolizinyl,  
(V) indazolyl,  
(W) benzothiazolyl,  
(X) benzimidazolyl,  
(Y) benzofuranyl,  
(Z) furanyl,  
(AA) thienyl,  
(BB) pyrrolyl,  
(CC) oxadiazolyl,  
(DD) thiadiazolyl,  
(EE) triazolyl,  
(FF) tetrazolyl,  
(GG) 1, 4-benzodioxan  
(HH) purinyl,  
(II) oxazolopyridinyl,  
(JJ) imidazopyridinyl,  
(KK) isothiazolyl,  
(LL) naphthyridinyl,  
(MM) cinnolinyl,  
(NN) carbazolyl,  
(OO)  $\beta$ -carbolinyl,  
(PP) isochromanyl,  
(QQ) chromanyl,  
(RR) furazanyl,  
(SS) tetrahydroisoquinoline,  
(TT) isoindolinyl,  
(UU) isobenzotetrahydrofuranyl,  
(VV) isobenzotetrahydrothienyl,  
(WW) isobenzothiophenyl,  
(XX) benzoxazolyl, or  
(YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}$  by any ring atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1$ - $C_3$  alkoxy,
- (5)  $-O-CF_3$ ,
- (6)  $-NH_2$ ,
- (7)  $-OH$ , or
- (8)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and

$R_{1\text{-heterocycle}}$  is:

- (A) morpholinyl,
- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or

two:

- (1) =O,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) -CF<sub>3</sub>,
- (4) -F, Cl, -Br and -I,
- (5) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (6) -O-CF<sub>3</sub>,
- (7) -NH<sub>2</sub>,
- (8) -OH, or
- (9) -C≡N,

with the proviso that when n<sub>1</sub> is zero R<sub>1-heterocycle</sub> is not bonded to the carbon chain by nitrogen;

where R<sub>2</sub> is:

- (I) -H,
- (II) C<sub>1</sub>-C<sub>6</sub> alkyl, or
- (III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub>  
where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above,

where R<sub>N</sub> is:

- (I) R<sub>N-1</sub>-X<sub>N</sub> where X<sub>N</sub> is:
  - (A) -CO-,
  - (B) -SO<sub>2</sub>-,
  - (C) -(CR'R'')<sub>1-6</sub> where R' and R'' are the same or different and are -H or C<sub>1</sub>-C<sub>4</sub> alkyl,
  - (D) -CO-(CR'R'')<sub>1-6</sub>-X<sub>N-1</sub> where X<sub>N-1</sub> is -O-, -S- and -NR'R''- and where R' and R'' are as defined above,
  - (E) a single bond;

where R<sub>N-1</sub> is:

- (A) R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1) C<sub>1</sub>-C<sub>6</sub> alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,
  - (c) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with one to three -F, -Cl, -Br, or -I,
  - (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
  - (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
  - (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
  - (g) -C<sub>1</sub>-C<sub>6</sub> alkenyl with one or two double bonds,
  - (h) -C<sub>1</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,
  - (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
  - (j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or
  - (k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,
- (8) -CO-(C<sub>3</sub>-C<sub>12</sub> alkyl),
- (9) -CO-(C<sub>3</sub>-C<sub>6</sub> cycloalkyl),
- (10) -CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,
- (11) -CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as defined above,
- (12) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each

group is unsubstituted or substituted with one or two  
C<sub>1</sub>-C<sub>3</sub> alkyl,

(13) -CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is:

(a) C<sub>1</sub>-C<sub>6</sub> alkyl, or

(b) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-aryl</sub>) where R<sub>1-aryl</sub> is as defined  
above,

(14) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined  
above,

(15) -SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(16) -SO<sub>2</sub>-(C<sub>3</sub>-C<sub>12</sub> alkyl),

(17) -NH-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,

(18) -NH-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(19) -N-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(20) -N(C<sub>1</sub>-C<sub>3</sub> alkyl)-CO-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined  
above,

(21) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or  
different and are as defined above,

(22) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(23) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(24) -O-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(25) -O-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(26) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(27) -O-(C<sub>2</sub>-C<sub>5</sub> alkyl)-COOH,

(28) -S-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(29) C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with 1, 2, 3, 4,  
or 5 -F,

(30) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with 1, 2,  
3, 4, or 5 -F, or

(31) -O-φ,

(B) -R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is:

(A) pyridinyl,

- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyl,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thienyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,



(GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C $\equiv$ N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:

- (a) -H,
- (b) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with one
- (i) -OH, or
- (ii) -NH<sub>2</sub>,
- (c) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with 1, 2, or 3 -F, -Cl, -Br, or -I,
- (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
- (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
- (g) -C<sub>1</sub>-C<sub>6</sub> alkenyl with one or two double bonds,
- (h) -C<sub>1</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,
- (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
- (j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or
- (k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,

(8) -CO-(C<sub>3</sub>-C<sub>12</sub> alkyl),

(9) -CO-(C<sub>3</sub>-C<sub>6</sub> cycloalkyl),

(10) -CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined above,

(11) -CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as defined above,

(12) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C<sub>1</sub>-C<sub>3</sub> alkyl,

(13) -CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is:

(a) C<sub>1</sub>-C<sub>6</sub> alkyl, or

(b) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-aryl</sub>) where R<sub>1-aryl</sub> is as defined above,

(14) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined above,

(15) -SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(16) -SO<sub>2</sub>-(C<sub>3</sub>-C<sub>12</sub> alkyl),

(17) -NH-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,

(18) -NH-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(19) -N-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(20) -N(C<sub>1</sub>-C<sub>3</sub> alkyl)-CO-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,

(21) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or different and are as defined above,

(22) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(23) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(24) -O-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(25) -O-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(26) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(27) -O-(C<sub>2</sub>-C<sub>5</sub> alkyl)-COOH, or

(28) -S-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(C) -R<sub>N-aryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(D) -R<sub>N-aryl</sub>-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(E) -R<sub>N-heteroaryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(F) -R<sub>N-heteroaryl</sub>-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(G) -R<sub>N-aryl</sub>-O-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(H) -R<sub>N-aryl</sub>-S-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

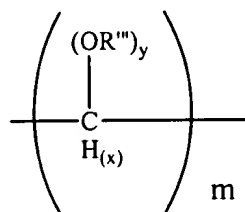
(I) -R<sub>N-heteroaryl</sub>-O-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

- (J)  $-R_{N\text{-heteroaryl}}-S-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,  
 (K)  $-R_{N\text{-aryl}}-\text{CO}-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,  
 (L)  $-R_{N\text{-aryl}}-\text{CO}-R_{N\text{-heteroaryl}}$  where  $-R_{N\text{-aryl}}$  and  $R_{N\text{-heteroaryl}}$  are as defined above,  
 (M)  $-R_{N\text{-aryl}}-\text{SO}_2-R_{N\text{-aryl}}$  where  $-R_{N\text{-aryl}}$  is as defined above,  
 (N)  $-R_{N\text{-heteroaryl}}-\text{CO}-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,  
 (O)  $-R_{N\text{-heteroaryl}}-\text{SO}_2-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,  
 (P)  $-R_{N\text{-aryl}}-\text{O}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,  
 (Q)  $-R_{N\text{-aryl}}-S-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,  
 (R)  $-R_{N\text{-heteroaryl}}-\text{O}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or  
 (S)  $-R_{N\text{-heteroaryl}}-S-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $A-X_N-$  where  $X_N$  is  $-\text{CO}-$ ,

wherein A is

- (A)  $-T-E-(Q)_m$ ,  
 (1) where  $-T$  is



where

- (a)  $x=1$  when  $y=1$  and  $x=2$  when  $y=0$ ,  
 (b)  $m$  is 0, 1, 2 or 3,  
 (c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and  
 (d)  $R'''$  varies independently on each carbon and is H,  $(\text{C}_1\text{-C}_2)$  alkyl, phenyl, or phenyl $(\text{C}_1\text{-C}_3)$ alkyl;

(2) -E is

- (a) C<sub>1</sub>-C<sub>5</sub> alkyl, but only if m' does not equal 0,
- (b) methylthioxy(C<sub>2</sub>-C<sub>4</sub>)alkyl,
- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,

- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
  - (m) heterocyclacyl,
  - (n) heteroarylacyl, or
  - (o) hydroxyl;
- (4) m' is 0, 1, 2 or 3;

- (B) -E(Q)<sub>m</sub> wherein E and -Q are as defined as above and m is 0, 1, 2, or 3;
- (C) -T-E wherein -E and -Q are as defined as above; or
- (D) -E wherein -E is as defined as above;

(III) -CO-(C<sub>1</sub>-C<sub>6</sub> alkyl) where alkyl is unsubstituted or substituted with one or two:

- (A) -OH,
- (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
- (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,
- (E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,
- (K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub> is the same or different and are as defined above, or

- (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,
- (IV) -CO-(C<sub>1</sub>-C<sub>3</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl) where alkyl is unsubstituted or substituted with one or two
- (A) -OH,
  - (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,
  - (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
  - (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,
  - (E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
  - (F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
  - (G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),
  - (H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
  - (I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
  - (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,
  - (K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
  - (L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
  - (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
  - (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub> are the same or different and are as defined above, or
  - (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,
- (V) -CO-(C<sub>1</sub>-C<sub>3</sub> alkyl)-S-(C<sub>1</sub>-C<sub>3</sub> alkyl) where alkyl is unsubstituted or substituted with one or two
- (A) -OH,
  - (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,
  - (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
  - (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,
  - (E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
  - (F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,  
 (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,  
 (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,  
 (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,  
 (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,  
 (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,  
 (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,  
 (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or  
 (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,  
 (VI)  $-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{\text{N-10}})-(\text{CH}_2)_{0-2}-\text{R}_{\text{N-aryl}}/\text{R}_{\text{N-heteroaryl}}$  where  $\text{R}_{\text{N-aryl}}$  and  $\text{R}_{\text{N-heteroaryl}}$  are as defined above, where  $\text{R}_{\text{N-10}}$  is:
- (A)  $-\text{H}$ ,  
 (B)  $\text{C}_1-\text{C}_6 \text{ alkyl}$ ,  
 (C)  $\text{C}_3-\text{C}_7 \text{ cycloalkyl}$ ,  
 (D)  $\text{C}_2-\text{C}_6 \text{ alkenyl}$  with one double bond,  
 (E)  $\text{C}_2-\text{C}_6 \text{ alkynyl}$  with one triple bond,  
 (F)  $\text{R}_{1-\text{aryl}}$  where  $\text{R}_{1-\text{aryl}}$  is as defined above, or  
 (G)  $\text{R}_{\text{N-heteroaryl}}$  where  $\text{R}_{\text{N-heteroaryl}}$  is as defined above;

where B is  $-\text{O}-$ ,  $-\text{NH}-$ , or  $-\text{N}(\text{C}_1-\text{C}_6 \text{ alkyl})-$ ;

where  $\text{R}_\text{C}$  is:

- (I)  $-(\text{C}_1-\text{C}_{10})\text{alkyl}-\text{K}_{1-3}$  in which:
- (A) the alkyl chain is unsubstituted or substituted with one  $-\text{OH}$ ,  
 (B) the alkyl chain is unsubstituted or substituted with one  $\text{C}_1-\text{C}_6$  alkoxy unsubstituted or substituted with 1-5  $-\text{F}$ ,  
 (C) the alkyl chain is unsubstituted or substituted with one  $-\text{O}-\phi$ ,  
 (D) the alkyl chain is unsubstituted or substituted with 1-5  $-\text{F}$ ,



(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

- (1) H,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II)-(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III)  $-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A)  $C_1-C_3$  alkyl unsubstituted or substituted with 1, 2, 3, or 4  $-F$ ,  
 $-Cl$ ,  $-Br$ , or  $-I$ ,

(B)  $-CO-OH$ ,

(C)  $-CO-O-(C_1-C_4 \text{ alkyl})$ ,

(D)  $-OH$ , or

(E)  $C_1-C_6$  alkoxy,

(IV)  $-(CH_2)_{2-6}-OH$ ,

(V)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-x}$  and  $R_{C-y}$  are  $-H$ ,  $C_1-C_4$  alkyl and  $\phi$ -  
and  $R_{C-aryl}$  is the same as  $R_{N-aryl}$ ,

(VI)  $-(CH_2)_{0-4}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,  
(U) benzimidazolyl,  
(V) benzofuranyl,  
(W) furanyl,  
(X) thienyl,  
(Y) pyrrolyl,  
(Z) oxadiazolyl,  
(AA) thiadiazolyl,  
(BB) triazolyl,  
(CC) tetrazolyl,  
(DD) 1, 4-benzodioxan  
(EE) purinyl,  
(FF) oxazolopyridinyl,  
(GG) imidazopyridinyl,  
(HH) isothiazolyl,  
(II) naphthyridinyl,  
(JJ) cinnolinyl,  
(KK) carbazolyl,  
(LL)  $\beta$ -carbolinyl,  
(MM) isochromanyl,  
(NN) chromanyl,  
(OO) furazanyl,  
(PP) tetrahydroisoquinoline,  
(QQ) isoindolinyl,  
(RR) isobenzotetrahydrofuranyl,  
(SS) isobenzotetrahydrothienyl,  
(TT) isobenzothiophenyl,  
(UU) benzoxazolyl, or  
(VV) pyridopyridinyl,  
(VII)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is the same as  $\text{R}_{\text{I-heterocycle}}$ ,

(VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:

- (A) -H,
- (B)  $-C_1-C_6$  alkyl,
- (C)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above for  $R_{1-aryl}$ ,
- (D)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (E)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (F)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (G)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (H)  $-(CH_2)_{1-4}-OH$ ,
- (I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'-aryl}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$ ,  $-NH-$  or  $-NHR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'-aryl}$  is as defined above,
- (J)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C-heteroaryl}$  where  $R_{C-4}$  and  $R_{C-heteroaryl}$  are as defined above, or
- (K)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,

and where  $R_{C-3}$  is:

- (A) -H,
  - (B)  $-C_1-C_6$  alkyl,
  - (C)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,
  - (D)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
  - (E)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
  - (F)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,
  - (G)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- or
- (H)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(IX)  $-CH(\phi)_2$ ,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (B) -CF<sub>3</sub>,
- (C) -F, Cl, -Br and -I,
- (D) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (E) -OCF<sub>3</sub>,
- (F) -NH<sub>2</sub>,
- (G) -OH, or
- (H) -C≡N,

(XI) -CH<sub>2</sub>-C≡CH;

(XII) -(CH<sub>2</sub>)<sub>0-1</sub>-CH(R<sub>C-5</sub>)-(CH<sub>2</sub>)<sub>0-1</sub>-φ where R<sub>C-5</sub> is:

- (A) -OH, or
- (B) -CH<sub>2</sub>-OH;

(XIII) -CH(-φ)-CO-O(C<sub>1</sub>-C<sub>3</sub> alkyl);

(XIV) -CH(-CH<sub>2</sub>-OH)-CH(-OH)-φ-NO<sub>2</sub>;

(XV) -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-OH;

(XVI) -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH(-O-CH<sub>2</sub>-CH<sub>3</sub>)<sub>2</sub>;

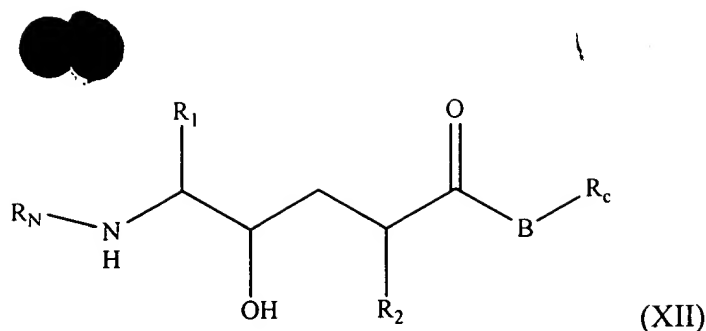
(XVII) -(C<sub>2</sub>-C<sub>8</sub>) alkynyl; or

(XVIII) -H; or a pharmaceutically acceptable salt thereof.

45. The method of claim 44, wherein said administering is to an animal.

46. The method of claim 45, wherein said administering is to a human.

47. A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a hydroxyethylene compound of the formula



where  $R_1$  is:

- (I)  $C_1$ - $C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, - $NH_2$ , -C $\equiv$ N, -CF $_3$ , or -N $_3$ ,
- (II)  $-(CH_2)_{1-2}$ -S-CH $_3$ ,
- (III)  $-CH_2$ -CH $_2$ -S-CH $_3$ ,
- (IV)  $-CH_2$ -( $C_2$ - $C_6$  alkenyl) unsubstituted or substituted by one -F,
- (V)  $-(CH_2)_{0-3}$ -( $R_{1-aryl}$ ) where  $R_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:
  - (A)  $C_1$ - $C_3$  alkyl,
  - (B) -CF $_3$ ,
  - (C) -F, Cl, -Br and -I,
  - (D)  $C_1$ - $C_3$  alkoxy,
  - (E) -O-CF $_3$ ,
  - (F) -NH $_2$ ,
  - (G) -OH, or
  - (H) -C $\equiv$ N,
- (VI)  $-(CH_2)_{n1}$ -( $R_{1-heteroaryl}$ ) where  $n_1$  is 0, 1, 2, or 3 and  $R_{1-heteroaryl}$  is:
  - (A) pyridinyl,
  - (B) pyrimidinyl,
  - (C) quinolinyl,
  - (D) indenyl,
  - (E) indanyl,
  - (F) benzothiophenyl,

(G) indolyl,  
(H) indolinyl,  
(I) pyridazinyl,  
(J) pyrazinyl,  
(K) isoindolyl,  
(L) isoquinolyl,  
(M) quinazolinyl,  
(N) quinoxalinyl,  
(O) phthalazinyl,  
(P) imidazolyl,  
(Q) isoxazolyl,  
(R) pyrazolyl,  
(S) oxazolyl,  
(T) thiazolyl,  
(U) indolizinyly,  
(V) indazolyl,  
(W) benzothiazolyl,  
(X) benzimidazolyl,  
(Y) benzofuranyl,  
(Z) furanyl,  
(AA) thienyl,  
(BB) pyrrolyl,  
(CC) oxadiazolyl,  
(DD) thiadiazolyl,  
(EE) triazolyl,  
(FF) tetrazolyl,  
(GG) 1, 4-benzodioxan  
(HH) purinyl,  
(II) oxazolopyridinyl,  
(JJ) imidazopyridinyl,  
(KK) isothiazolyl,

(LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanlyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1-C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1-C_3$  alkoxy,
- (5)  $-O-CF_3$ ,
- (6)  $-NH_2$ ,
- (7)  $-OH$ , or
- (8)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and

$R_{1\text{-heterocycle}}$  is:

(A) morpholinyl,



- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2)  $C_1\text{-}C_3$  alkyl,
- (3)  $-CF_3$ ,
- (4) -F, Cl, -Br and -I,
- (5)  $C_1\text{-}C_3$  alkoxy,
- (6)  $-O-CF_3$ ,
- (7)  $-NH_2$ ,
- (8) -OH, or
- (9)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $R_2$  is:

- (I) -H,
- (II)  $C_1\text{-}C_6$  alkyl, or
- (III)  $-(CH_2)_{0-4}\text{-}R_{2-1}$  where  $R_{2-1}$  is  $(C_3\text{-}C_6)\text{cycloalkyl}$ ,  $R_{1\text{-aryl}}$  or  $R_{1\text{-heteroaryl}}$

where  $R_{1\text{-aryl}}$  and  $R_{1\text{-heteroaryl}}$  are as defined above,

where  $R_N$  is:

(I)  $R_{N-1}-X_N$ - where  $X_N$  is:

- (A)  $-\text{CO}-$ ,
- (B)  $-\text{SO}_2-$ ,
- (C)  $-(\text{CR}'\text{R}'')_{1-6}$  where  $\text{R}'$  and  $\text{R}''$  are the same or different and are  $-\text{H}$  or  $\text{C}_1-\text{C}_4$  alkyl,
- (D)  $-\text{CO}-(\text{CR}'\text{R}'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'\text{R}''-$  and where  $\text{R}'$  and  $\text{R}''$  are as defined above,
- (E) a single bond;

where  $R_{N-1}$  is:

(A)  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1)  $\text{C}_1-\text{C}_6$  alkyl,
- (2)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,
- (3)  $-\text{OH}$ ,
- (4)  $-\text{NO}_2$ ,
- (5)  $-\text{CO}-\text{OH}$ ,
- (6)  $-\text{C}\equiv\text{N}$ ,
- (7)  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where  $\text{R}_{N-2}$  and  $\text{R}_{N-3}$  are the same or different and are:
  - (a)  $-\text{H}$ ,
  - (b)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one
    - (i)  $-\text{OH}$ , or
    - (ii)  $-\text{NH}_2$ ,
  - (c)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one to three  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,
  - (d)  $-\text{C}_3-\text{C}_7$  cycloalkyl,
  - (e)  $-(\text{C}_1-\text{C}_2 \text{ alkyl})-(\text{C}_3-\text{C}_7 \text{ cycloalkyl})$ ,

- (f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,
- (g)  $-C_1-C_6 \text{ alkenyl}$  with one or two double bonds,
- (h)  $-C_1-C_6 \text{ alkynyl}$  with one or two triple bonds,
- (i)  $-C_1-C_6 \text{ alkyl chain}$  with one double bond and one triple bond,
- (j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, or
- (k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,
- (8)  $-CO-(C_3-C_{12} \text{ alkyl})$ ,
- (9)  $-CO-(C_3-C_6 \text{ cycloalkyl})$ ,
- (10)  $-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,
- (11)  $-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,
- (12)  $-CO-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3 \text{ alkyl}$ ,
- (13)  $-CO-O-R_{N-5}$  where  $R_{N-5}$  is:
  - (a)  $C_1-C_6 \text{ alkyl}$ , or
  - (b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,
- (14)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,
- (15)  $-SO-(C_1-C_8 \text{ alkyl})$ ,
- (16)  $-SO_2-(C_3-C_{12} \text{ alkyl})$ ,
- (17)  $-NH-CO-O-R_{N-5}$  where  $R_{N-5}$  is as defined above,
- (18)  $-NH-CO-N(C_1-C_3 \text{ alkyl})_2$ ,
- (19)  $-N-CS-N(C_1-C_3 \text{ alkyl})_2$ ,
- (20)  $-N(C_1-C_3 \text{ alkyl})-CO-R_{N-5}$  where  $R_{N-5}$  is as defined above,
- (21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,
- (22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

- (23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,
- (24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,
- (25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,
- (26)  $-O-(C_1-C_6 \text{ alkyl})$ ,
- (27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ ,
- (28)  $-S-(C_1-C_6 \text{ alkyl})$ ,
- (29)  $C_1-C_6 \text{ alkyl}$  unsubstituted or substituted with 1, 2, 3, 4, or 5  $-F$ ,
- (30)  $-O-(C_1-C_6 \text{ alkyl}$  unsubstituted or substituted with 1, 2, 3, 4, or 5  $-F$ , or
- (31)  $-O-\phi$ ,

(B)  $-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,

(T) thiazolyl,  
 (U) indolizinyll,  
 (V) indazolyl,  
 (W) benzothiazolyl,  
 (X) benzimidazolyl,  
 (Y) benzofuranyl,  
 (Z) furanyl,  
 (AA) thienyl,  
 (BB) pyrrolyl,  
 (CC) oxadiazolyl,  
 (DD) thiadiazolyl,  
 (EE) triazolyl,  
 (FF) tetrazolyl,  
 (GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanlyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (3)  $-OH$ ,
- (4)  $-NO_2$ ,
- (5)  $-CO-OH$ ,
- (6)  $-C\equiv N$ ,
- (7)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are:
  - (a)  $-H$ ,
  - (b)  $-C_1\text{-}C_6$  alkyl unsubstituted or substituted with one
    - (i)  $-OH$ , or
    - (ii)  $-NH_2$ ,
  - (c)  $-C_1\text{-}C_6$  alkyl unsubstituted or substituted with 1, 2, or 3  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
  - (d)  $-C_3\text{-}C_7$  cycloalkyl,
  - (e)  $-(C_1\text{-}C_2\text{ alkyl})-(C_3\text{-}C_7\text{ cycloalkyl})$ ,
  - (f)  $-(C_1\text{-}C_6\text{ alkyl})-O-(C_1\text{-}C_3\text{ alkyl})$ ,
  - (g)  $-C_1\text{-}C_6$  alkenyl with one or two double bonds,
  - (h)  $-C_1\text{-}C_6$  alkynyl with one or two triple bonds,
  - (i)  $-C_1\text{-}C_6$  alkyl chain with one double bond and one triple bond,
  - (j)  $-R_{1\text{-aryl}}$  where  $R_{1\text{-aryl}}$  is as defined above, or

(k)  $-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,

(8)  $-\text{CO}-(\text{C}_3\text{-C}_{12} \text{ alkyl})$ ,

(9)  $-\text{CO}-(\text{C}_3\text{-C}_6 \text{ cycloalkyl})$ ,

(10)  $-\text{CO}-R_{1\text{-heteroaryl}}$  where  $R_{1\text{-heteroaryl}}$  is as defined above,

(11)  $-\text{CO}-R_{1\text{-heterocycle}}$  where  $R_{1\text{-heterocycle}}$  is as defined above,

(12)  $-\text{CO}-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $\text{C}_1\text{-C}_3$  alkyl,

(13)  $-\text{CO}-\text{O}-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $\text{C}_1\text{-C}_6$  alkyl, or

(b)  $-(\text{CH}_2)_{0-2}-(R_{1\text{-aryl}})$  where  $R_{1\text{-aryl}}$  is as defined above,

(14)  $-\text{SO}_2\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(15)  $-\text{SO}-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,

(16)  $-\text{SO}_2-(\text{C}_3\text{-C}_{12} \text{ alkyl})$ ,

(17)  $-\text{NH}-\text{CO}-\text{O}-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(18)  $-\text{NH}-\text{CO}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(19)  $-\text{N}-\text{CS}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(20)  $-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})-\text{CO}-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(21)  $-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-\text{O}-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,

(24)  $-\text{O}-\text{CO}-\text{N}(\text{C}_1\text{-C}_3 \text{ alkyl})_2$ ,

(25) -O-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,

(26) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(27) -O-(C<sub>2</sub>-C<sub>5</sub> alkyl)-COOH, or

(28) -S-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(C) -R<sub>N-aryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(D) -R<sub>N-aryl</sub>-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(E) -R<sub>N-heteroaryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(F) -R<sub>N-heteroaryl</sub>-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(G) -R<sub>N-aryl</sub>-O-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(H) -R<sub>N-aryl</sub>-S-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(I) -R<sub>N-heteroaryl</sub>-O-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(J) -R<sub>N-heteroaryl</sub>-S-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(K) -R<sub>N-aryl</sub>-CO-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(L) -R<sub>N-aryl</sub>-CO-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and R<sub>N-heteroaryl</sub> are as defined above,

(M) -R<sub>N-aryl</sub>-SO<sub>2</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(N) -R<sub>N-heteroaryl</sub>-CO-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(O) -R<sub>N-heteroaryl</sub>-SO<sub>2</sub>-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(P) -R<sub>N-aryl</sub>-O-(C<sub>1</sub>-C<sub>8</sub> alkyl)-φ where R<sub>N-aryl</sub> is as defined above,

(Q) -R<sub>N-aryl</sub>-S-(C<sub>1</sub>-C<sub>8</sub> alkyl)-φ where R<sub>N-aryl</sub> is as defined above,

(R) -R<sub>N-heteroaryl</sub>-O-(C<sub>1</sub>-C<sub>8</sub> alkyl)-φ where R<sub>N-heteroaryl</sub> is as defined above, or

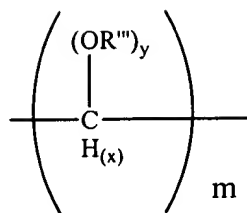
(S) -R<sub>N-heteroaryl</sub>-S-(C<sub>1</sub>-C<sub>8</sub> alkyl)-φ where R<sub>N-heteroaryl</sub> is as defined above,

(II) A-X<sub>N</sub>- where X<sub>N</sub> is -CO-,

wherein A is



- (A) -T-E-(Q)<sub>m'</sub>,  
 (1) where -T is



where

- (a) x = 1 when y = 1 and x = 2 when y = 0,
- (b) m is 0, 1, 2 or 3,
- (c) the values of x and y vary independently on each carbon when m is 2 and 3, and
- (d) R''' varies independently on each carbon and is H, (C<sub>1</sub>-C<sub>2</sub>) alkyl, phenyl, or phenyl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

(2) -E is

- (a) C<sub>1</sub>-C<sub>5</sub> alkyl, but only if m' does not equal 0,
- (b) methylthioxy(C<sub>2</sub>-C<sub>4</sub>)alkyl,
- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,

- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclylacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4)  $m'$  is 0, 1, 2 or 3;

(III)  $-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two:

- (E)  $-\text{CO}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is as defined above,
- (K)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N}-8}\text{R}_{\text{N}-8}$  where the  $\text{R}_{\text{N}-8}$  is the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,
- (IV)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is as defined above,
- (K)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,

- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or  
 (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,  
 (V)  $-CO-(C_1-C_3 \text{ alkyl})-S-(C_1-C_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two

- (A)  $-OH$ ,  
 (B)  $-C_1-C_6 \text{ alkoxy}$ ,  
 (C)  $-C_1-C_6 \text{ thioalkoxy}$ ,  
 (D)  $-CO-O-R_{N-8}$  where  $R_{N-8}$  is  $-H$ ,  $C_1-C_6 \text{ alkyl}$  or  $-\phi$ ,  
 (E)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (F)  $-CO-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (G)  $-SO_2-(C_1-C_8 \text{ alkyl})$ ,  
 (H)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,  
 (I)  $-NH-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (J)  $-NH-CO-O-R_{N-8}$  where  $R_{N-8}$  is as defined above,  
 (K)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (M)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or  
 (O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,  
 (VI)  $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-R_{N-aryl}/R_{N-heteroaryl})$  where  $R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above, where  $R_{N-10}$  is:

- (A)  $-H$ ,  
 (B)  $C_1-C_6 \text{ alkyl}$ ,  
 (C)  $C_3-C_7 \text{ cycloalkyl}$ ,

- (D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,
- (E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,
- (F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or
- (G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above;

where B is -O-, -NH-, or -N(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

where R<sub>C</sub> is:

(I) -(C<sub>1</sub>-C<sub>10</sub>)alkyl-K<sub>1-3</sub> in which:

- (A) the alkyl chain is unsubstituted or substituted with one -OH,
- (B) the alkyl chain is unsubstituted or substituted with one C<sub>1</sub>-C<sub>6</sub> alkoxy unsubstituted or substituted with 1-5 -F,
- (C) the alkyl chain is unsubstituted or substituted with one -O-φ,
- (D) the alkyl chain is unsubstituted or substituted with 1-5 -F,
- (E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

- (1) H,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclacyl,

(15) heteroarylacyl,

(16) amino unsubstituted or substituted with  $C_1$ - $C_6$  alkyl,

(17) hydroxyl, or

(18) carboxyl methyl ester;

(II)  $-(CH_2)_{0-3}-J-[-(CH_2)_{0-3}-K]_{1-3}$  where K is as defined above and J is:

(A) a 5 to 7 atom monocyclic aryl group,

(B) a 8 to 12 atom multicyclic aryl group,

(C) a 5 to 7 atom heterocyclic group,

(D) a 8 to 12 atom multicyclic heterocyclic group, or

(E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III)  $-(CH_2)_{0-3}-(C_3-C_7)$  cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A)  $C_1$ - $C_3$  alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O- $(C_1-C_4)$  alkyl),

(D) -OH, or

(E)  $C_1$ - $C_6$  alkoxy,

(IV)  $-(CH_2)_{2-6}$ -OH,

(V)  $-(R_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-x}$  and  $R_{C-y}$  are -H,  $C_1$ - $C_4$  alkyl and  $\phi$ - and  $R_{C-aryl}$  is the same as  $R_{N-aryl}$ ,

(VI)  $-(CH_2)_{0-4}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

- (H) indolinyI,
- (I) pyridazinyI,
- (J) pyrazinyI,
- (K) isoindolyI,
- (L) isoquinolyI,
- (M) quinazolinyl,
- (N) quinoxalinyI,
- (O) phthalazinyI,
- (P) isoxazolyl,
- (Q) pyrazolyl,
- (R) indolizinyI,
- (S) indazolyl,
- (T) benzothiazolyl,
- (U) benzimidazolyl,
- (V) benzofuranyl,
- (W) furanyl,
- (X) thienyl,
- (Y) pyrrolyl,
- (Z) oxadiazolyl,
- (AA) thiadiazolyl,
- (BB) triazolyl,
- (CC) tetrazolyl,
- (DD) 1, 4-benzodioxan
- (EE) purinyI,
- (FF) oxazolopyridinyI,
- (GG) imidazopyridinyI,
- (HH) isothiazolyl,
- (II) naphthyridinyI,
- (JJ) cinnolinyI,
- (KK) carbazolyl,
- (LL)  $\beta$ -carbolinyI,

(MM) isochromanyl,  
 (NN) chromanyl,  
 (OO) furazanyl,  
 (PP) tetrahydroisoquinoline,  
 (QQ) isoindolinyI,  
 (RR) isobenzotetrahydrofuranyl,  
 (SS) isobenzotetrahydrothienyl,  
 (TT) isobenzothiophenyl,  
 (UU) benzoxazolyI, or  
 (VV) pyridopyridinyI,

(VII)  $-(CH_2)_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-heterocycle}$ ,

(VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:

- (A) -H,
- (B)  $-C_1-C_6$  alkyl,
- (C)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above for  $R_{1-aryl}$ ,
- (D)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (E)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (F)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
- (G)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
- (H)  $-(CH_2)_{1-4}-OH$ ,
- (I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'-aryl}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$ ,  $-NH-$  or  $-NHR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'-aryl}$  is as defined above,
- (J)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C-heteroaryl}$  where  $R_{C-4}$  and  $R_{C-heteroaryl}$  are as defined above, or
- (K)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,

and where  $R_{C-3}$  is:

- (A) -H,



- (B)  $-C_1-C_6$  alkyl,  
 (C)  $-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,  
 (D)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,  
 (E)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,  
 (F)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above,  
 (G)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,

or

- (H)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,

(IX)  $-CH(\phi)_2$ ,

(X) -cyclopentyl or -cyclohexyl ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

- (A)  $C_1-C_3$  alkyl,  
 (B)  $-CF_3$ ,  
 (C)  $-F$ ,  $Cl$ ,  $-Br$  and  $-I$ ,  
 (D)  $C_1-C_3$  alkoxy,  
 (E)  $-OCF_3$ ,  
 (F)  $-NH_2$ ,  
 (G)  $-OH$ , or  
 (H)  $-C\equiv N$ ,

(XI)  $-CH_2-C\equiv CH$ ;

(XII)  $-(CH_2)_{0-1}-CHR_{C-5}-(CH_2)_{0-1}-\phi$  where  $R_{C-5}$  is:

- (A)  $-OH$ , or  
 (B)  $-CH_2-OH$ ;

(XIII)  $-CH(-\phi)-CO-O(C_1-C_3 \text{ alkyl})$ ;

(XIV)  $-CH(-CH_2-OH)-CH(-OH)-\phi-NO_2$ ;

(XV)  $-(CH_2)_2-O-(CH_2)_2-OH$ ;

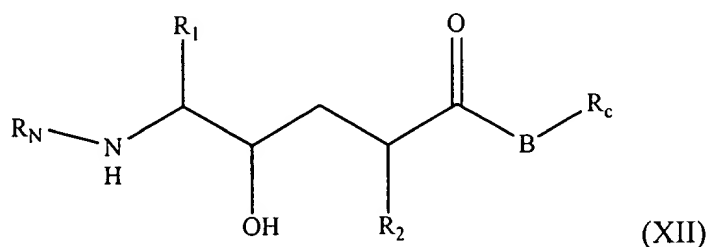
(XVI)  $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$ ;

(XVII)  $-(C_2-C_8 \text{ alkynyl})$ ; or

(XVIII)  $-H$ ; or a pharmaceutically acceptable salt thereof.

48. The method of claim 47, wherein said animal is a human.

49. A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a hydroxyethylene compound of the formula



where  $R_1$  is:

(I)  $C_1$ - $C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, - $NH_2$ , -C $\equiv$ N, -CF $_3$ , or -N $_3$ ,

(II) -(CH $_2$ ) $_{1-2}$ -S-CH $_3$ ,

(III) -CH $_2$ -CH $_2$ -S-CH $_3$ ,

(IV) -CH $_2$ -( $C_2$ - $C_6$  alkenyl) unsubstituted or substituted by one -F,

(V) -(CH $_2$ ) $_{0-3}$ -( $R_{1-aryl}$ ) where  $R_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A)  $C_1$ - $C_3$  alkyl,

(B) -CF $_3$ ,

(C) -F, Cl, -Br and -I,

(D)  $C_1$ - $C_3$  alkoxy,

(E) -O-CF $_3$ ,

(F) -NH $_2$ ,

(G) -OH, or

(H) -C $\equiv$ N,

(VI) -(CH $_2$ ) $_{n_1}$ -( $R_{1-heteroaryl}$ ) where  $n_1$  is 0, 1, 2, or 3 and  $R_{1-heteroaryl}$  is:

(A) pyridinyl,

- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyll,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thienyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,

(GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanlyl,  
 (QQ) chromanlyl,  
 (RR) furazanlyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1$ - $C_3$  alkoxy,
- (5)  $-O-CF_3$ ,
- (6)  $-NH_2$ ,
- (7)  $-OH$ , or
- (8)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $-(CH_2)_{n_1}-(R_{1\text{-heterocycle}})$  where  $n_1$  is as defined above and

$R_{1\text{-heterocycle}}$  is:

- (A) morpholinyl,
- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2)  $C_1$ - $C_3$  alkyl,
- (3)  $-CF_3$ ,
- (4) -F, Cl, -Br and -I,
- (5)  $C_1$ - $C_3$  alkoxy,
- (6)  $-O-CF_3$ ,
- (7)  $-NH_2$ ,
- (8) -OH, or
- (9)  $-C\equiv N$ ,

with the proviso that when  $n_1$  is zero  $R_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $R_2$  is:

- (I) -H,
- (II)  $C_1-C_6$  alkyl, or
- (III)  $-(CH_2)_{0-4}-R_{2-1}$  where  $R_{2-1}$  is  $(C_3-C_6)$ cycloalkyl,  $R_{1-aryl}$  or  $R_{1-heteroaryl}$

where  $R_{1-aryl}$  and  $R_{1-heteroaryl}$  are as defined above,

where  $R_N$  is:

(I)  $R_{N-1}-X_N$  where  $X_N$  is:

- (A)  $-CO-$ ,
- (B)  $-SO_2-$ ,
- (C)  $-(CR'R'')_{1-6}$  where  $R'$  and  $R''$  are the same or different and are  $-H$  or  $C_1-C_4$  alkyl,
- (D)  $-CO-(CR'R'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is  $-O-$ ,  $-S-$  and  $-NR'R''-$  and where  $R'$  and  $R''$  are as defined above,
- (E) a single bond;

where  $R_{N-1}$  is:

(A)  $R_{N-aryl}$  where  $R_{N-aryl}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1)  $C_1-C_6$  alkyl,
- (2)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (3)  $-OH$ ,
- (4)  $-NO_2$ ,
- (5)  $-CO-OH$ ,
- (6)  $-C\equiv N$ ,
- (7)  $-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are:

- (a)  $-H$ ,
- (b)  $-C_1-C_6$  alkyl unsubstituted or substituted with one
  - (i)  $-OH$ , or

- (ii)  $\text{-NH}_2$ ,
- (c)  $\text{-C}_1\text{-C}_6$  alkyl unsubstituted or substituted with one to three  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ , or  $\text{-I}$ ,
- (d)  $\text{-C}_3\text{-C}_7$  cycloalkyl,
- (e)  $\text{-(C}_1\text{-C}_2\text{ alkyl)-(C}_3\text{-C}_7\text{ cycloalkyl)}$ ,
- (f)  $\text{-(C}_1\text{-C}_6\text{ alkyl)-O-(C}_1\text{-C}_3\text{ alkyl)}$ ,
- (g)  $\text{-C}_1\text{-C}_6$  alkenyl with one or two double bonds,
- (h)  $\text{-C}_1\text{-C}_6$  alkynyl with one or two triple bonds,
- (i)  $\text{-C}_1\text{-C}_6$  alkyl chain with one double bond and one triple bond,
- (j)  $\text{-R}_{1\text{-aryl}}$  where  $\text{R}_{1\text{-aryl}}$  is as defined above, or
- (k)  $\text{-R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-heteroaryl}}$  is as defined above,
- (8)  $\text{-CO-(C}_3\text{-C}_{12}\text{ alkyl)}$ ,
- (9)  $\text{-CO-(C}_3\text{-C}_6\text{ cycloalkyl)}$ ,
- (10)  $\text{-CO-R}_{1\text{-heteroaryl}}$  where  $\text{R}_{1\text{-heteroaryl}}$  is as defined above,
- (11)  $\text{-CO-R}_{1\text{-heterocycle}}$  where  $\text{R}_{1\text{-heterocycle}}$  is as defined above,
- (12)  $\text{-CO-R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $\text{C}_1\text{-C}_3$  alkyl,
- (13)  $\text{-CO-O-R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  is:
  - (a)  $\text{C}_1\text{-C}_6$  alkyl, or
  - (b)  $\text{-(CH}_2\text{)}_{0-2}\text{-(R}_{1\text{-aryl}}\text{)}$  where  $\text{R}_{1\text{-aryl}}$  is as defined above,
- (14)  $\text{-SO}_2\text{-NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are as defined above,
- (15)  $\text{-SO-(C}_1\text{-C}_8\text{ alkyl)}$ ,
- (16)  $\text{-SO}_2\text{-(C}_3\text{-C}_{12}\text{ alkyl)}$ ,
- (17)  $\text{-NH-CO-O-R}_{\text{N-5}}$  where  $\text{R}_{\text{N-5}}$  is as defined above,
- (18)  $\text{-NH-CO-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (19)  $\text{-N-CS-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,

(20)  $-N(C_1-C_3 \text{ alkyl})-CO-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,

(25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,

(26)  $-O-(C_1-C_6 \text{ alkyl})$ ,

(27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ ,

(28)  $-S-(C_1-C_6 \text{ alkyl})$ ,

(29)  $C_1-C_6$  alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5  $-F$ ,

(30)  $-O-(C_1-C_6 \text{ alkyl})$  unsubstituted or substituted with 1, 2, 3, 4, or 5  $-F$ , or

(31)  $-O-\phi$ ,

(B)  $-R_{N-\text{heteroaryl}}$  where  $R_{N-\text{heteroaryl}}$  is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,



- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyll,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thienyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,
- (GG) 1, 4-benzodioxan
- (HH) purinyl,
- (II) oxazolopyridinyl,
- (JJ) imidazopyridinyl,
- (KK) isothiazolyl,
- (LL) naphthyridinyl,
- (MM) cinnolinyl,
- (NN) carbazolyl,
- (OO)  $\beta$ -carbolinyl,
- (PP) isochromanyl,
- (QQ) chromanyl,
- (RR) furazanyl,
- (SS) tetrahydroisoquinoline,

(TT) isoindolinyI,  
 (UU) isobenzotetrahydrofuranyI,  
 (VV) isobenzotetrahydrothienyI,  
 (WW) isobenzothiophenyI,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyI,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b)  $C_1\text{-}C_6$  alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,
  - (c)  $C_1\text{-}C_6$  alkyl unsubstituted or substituted with 1, 2, or 3 -F, -Cl, -Br, or -I,
  - (d)  $C_3\text{-}C_7$  cycloalkyl,
  - (e) -( $C_1\text{-}C_2$  alkyl)-( $C_3\text{-}C_7$  cycloalkyl),
  - (f) -( $C_1\text{-}C_6$  alkyl)-O-( $C_1\text{-}C_3$  alkyl),
  - (g)  $C_1\text{-}C_6$  alkenyl with one or two double bonds,

(h)  $-C_1-C_6$  alkynyl with one or two triple bonds,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,  
or

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(8)  $-CO-(C_3-C_{12}$  alkyl),

(9)  $-CO-(C_3-C_6$  cycloalkyl),

(10)  $-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(11)  $-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,

(12)  $-CO-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3$  alkyl,

(13)  $-CO-O-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $C_1-C_6$  alkyl, or

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,

(14)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(15)  $-SO-(C_1-C_8$  alkyl),

(16)  $-SO_2-(C_3-C_{12}$  alkyl),

(17)  $-NH-CO-O-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(18)  $-NH-CO-N(C_1-C_3$  alkyl) $_2$ ,

(19)  $-N-CS-N(C_1-C_3$  alkyl) $_2$ ,

(20)  $-N(C_1-C_3 \text{ alkyl})-CO-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,

(24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,

(25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,

(26)  $-O-(C_1-C_6 \text{ alkyl})$ ,

(27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ , or

(28)  $-S-(C_1-C_6 \text{ alkyl})$ ,

(C)  $-R_{N-aryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(D)  $-R_{N-aryl}-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,

(E)  $-R_{N-heteroaryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,

(F)  $-R_{N-heteroaryl}-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(G)  $-R_{N-aryl}-O-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(H)  $-R_{N-aryl}-S-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(I)  $-R_{N-heteroaryl}-O-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(J)  $-R_{N-heteroaryl}-S-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(K)  $-R_{N-aryl}-CO-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(L)  $-R_{N-aryl}-CO-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above,

(M)  $-R_{N-aryl}-SO_2-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,

(N)  $-R_{N-heteroaryl}-CO-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(O)  $-R_{N-heteroaryl}-SO_2-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,

(P)  $-R_{N-aryl}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N-aryl}$  is as defined above,

(Q)  $-R_{N-aryl}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N-aryl}$  is as defined above,

(R)  $-R_{N\text{-heteroaryl}}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or

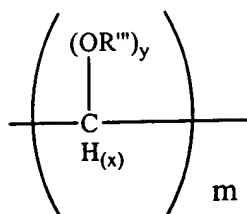
(S)  $-R_{N\text{-heteroaryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $A-X_N$ - where  $X_N$  is  $-CO-$ ,

wherein A is

(A)  $-T-E-(Q)_{m'}$ ,

(1) where  $-T$  is



where

(a)  $x=1$  when  $y=1$  and  $x=2$  when  $y=0$ ,

(b)  $m$  is 0, 1, 2 or 3,

(c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and

(d)  $R'''$  varies independently on each carbon and is H,  $(C_1-C_2)$  alkyl, phenyl, or phenyl $(C_1-C_3)$ alkyl;

(2)  $-E$  is

(a)  $C_1-C_5$  alkyl, but only if  $m'$  does not equal 0,

(b) methylthioxy $(C_2-C_4)$ alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -E(Q)<sub>m</sub>" wherein E and -Q are as defined as above and m" is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III)  $-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two:

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  is the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,

(IV)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,

(H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,

(K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,

(M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or

(O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,

(V)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{S}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two

(A)  $-\text{OH}$ ,

(B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,

(C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,

(D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,

(E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,

(G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,

(H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,

(K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,

(M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or



(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(VI) -CO-CH(-(CH<sub>2</sub>)<sub>0-2</sub>-O-R<sub>N-10</sub>)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>N-aryl</sub>/R<sub>N-heteroaryl</sub>) where R<sub>N-aryl</sub>

and R<sub>N-heteroaryl</sub> are as defined above, where R<sub>N-10</sub> is:

(A) -H,

(B) C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,

(E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,

(F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, or

(G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above;

where B is -O-, -NH-, or -N(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

where R<sub>C</sub> is:

(I) -(C<sub>1</sub>-C<sub>10</sub>)alkyl-K<sub>1-3</sub> in which:

(A) the alkyl chain is unsubstituted or substituted with one -OH,

(B) the alkyl chain is unsubstituted or substituted with one C<sub>1</sub>-C<sub>6</sub> alkoxy unsubstituted or substituted with 1-5 -F,

(C) the alkyl chain is unsubstituted or substituted with one -O-φ,

(D) the alkyl chain is unsubstituted or substituted with 1-5 -F,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1) H,

(2) C<sub>1</sub>-C<sub>3</sub> alkyl,

(3) C<sub>1</sub>-C<sub>3</sub> alkoxy,

(4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,

(5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,

(6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,

(7) amido

(8) C<sub>1</sub>-C<sub>6</sub> alkylamino

- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,
- (B) -CO-OH,
- (C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),
- (D) -OH, or
- (E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(IV) -(CH<sub>2</sub>)<sub>2-6</sub>-OH,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are -H, C<sub>1</sub>-C<sub>4</sub> alkyl and  $\phi$ - and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub>,

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is:

- (A) pyridinyl,

- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) isoxazolyl,
- (Q) pyrazolyl,
- (R) indolizinyl,
- (S) indazolyl,
- (T) benzothiazolyl,
- (U) benzimidazolyl,
- (V) benzofuranyl,
- (W) furanyl,
- (X) thienyl,
- (Y) pyrrolyl,
- (Z) oxadiazolyl,
- (AA) thiadiazolyl,
- (BB) triazolyl,
- (CC) tetrazolyl,
- (DD) 1, 4-benzodioxan
- (EE) purinyl,
- (FF) oxazolopyridinyl,

(GG) imidazopyridinyl,  
 (HH) isothiazolyl,  
 (II) naphthyridinyl,  
 (JJ) cinnolinyl,  
 (KK) carbazolyl,  
 (LL)  $\beta$ -carbolinyl,  
 (MM) isochromanlyl,  
 (NN) chromanlyl,  
 (OO) furazanlyl,  
 (PP) tetrahydroisoquinoline,  
 (QQ) isoindolinyl,  
 (RR) isobenzotetrahydrofuranyl,  
 (SS) isobenzotetrahydrothienyl,  
 (TT) isobenzothiophenyl,  
 (UU) benzoxazolyl, or  
 (VV) pyridopyridinyl,

(VII)  $-(CH_2)_{0-4}-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is the same as  $R_{I\text{-heterocycle}}$ ,

(VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:

(A) -H,

(B)  $-C_1-C_6$  alkyl,

(C)  $-(C_1-C_4 \text{ alkyl})-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above for  $R_{I\text{-aryl}}$ ,

(D)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(E)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(F)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(G)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(H)  $-(CH_2)_{1-4}-OH$ ,

(I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'\text{-aryl}}$  where  $R_{C-4}$  is -O-, -S-, -NH- or

$-\text{NHR}_{\text{C-5}}$  where  $\text{R}_{\text{C-5}}$  is  $\text{C}_1\text{-C}_6$  alkyl, and where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(J)  $-(\text{CH}_2)_{1-4}\text{-R}_{\text{C-4}}\text{-(CH}_2)_{1-4}\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-4}}$  and  $\text{R}_{\text{C-heteroaryl}}$  are as defined above, or

(K)  $-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

and where  $\text{R}_{\text{C-3}}$  is:

(A)  $-\text{H}$ ,

(B)  $-\text{C}_1\text{-C}_6$  alkyl,

(C)  $-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(D)  $-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(E)  $-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(F)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined above,

(G)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

or

(H)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is as defined above,

(IX)  $-\text{CH}(\phi)_2$ ,

(X)  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A)  $\text{C}_1\text{-C}_3$  alkyl,

(B)  $-\text{CF}_3$ ,

(C)  $-\text{F}$ ,  $\text{Cl}$ ,  $-\text{Br}$  and  $-\text{I}$ ,

(D)  $\text{C}_1\text{-C}_3$  alkoxy,

(E)  $-\text{OCF}_3$ ,

(F)  $-\text{NH}_2$ ,

(G)  $-\text{OH}$ , or

(H)  $-\text{C}\equiv\text{N}$ ,

(XI)  $-\text{CH}_2\text{-C}\equiv\text{CH}$ ;

(XII)  $-(\text{CH}_2)_{0-1}\text{-CHR}_{\text{C-5}}\text{-(CH}_2)_{0-1}\text{-}\phi$  where  $\text{R}_{\text{C-5}}$  is:

(A)  $-\text{OH}$ , or

(B)-CH<sub>2</sub>-OH; .

(XIII) -CH(-φ)-CO-O(C<sub>1</sub>-C<sub>3</sub> alkyl);

(XIV) -CH(-CH<sub>2</sub>-OH)-CH(-OH)-φ-NO<sub>2</sub>;

(XV) -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-OH;

(XVI) -CH<sub>2</sub>-NH-CH<sub>2</sub>-CH(-O-CH<sub>2</sub>-CH<sub>3</sub>)<sub>2</sub>;

(XVII) -(C<sub>2</sub>-C<sub>8</sub>) alkynyl; or

(XVIII) -H; or a pharmaceutically acceptable salt thereof.

50. The method of claim 49, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 0.1nM to about 200μM.

51. The method of claim 50, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 10nM to about 100μM.

52. The method of claim 51, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 100nM to about 50μM.

53. The method of claim 52, wherein said compound inhibits 50% of the enzyme's activity at a concentration of from about 1μM to about 10μM.

54. The method of claim 49, wherein said thereapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

55. The method of claim 49, wherein said thereapeutic amount is in the range of from about 15 to about 1500 mg/day.

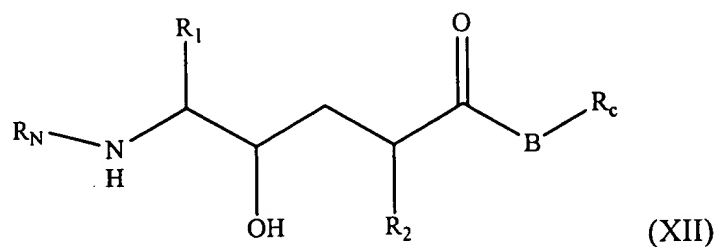
56. The method of claim 55, wherein said thereapeutic amount is in the range of from about 1 to about 100 mg/day.

57. The method of claim 56, wherein said thereapeutic amount is in the range of from about 5 to about 50 mg/day.

58. The method of claim 49, wherein said disease is Alzheimer's disease.

59. The method of claim 49, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

60. A composition comprising  $\beta$ -secretase complexed with a hydroxyethylene compound of the formula



where  $R_1$  is:

(I)  $C_1$ - $C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1$ - $C_3$  alkyl, -F, -Cl, -Br, -I, -OH, - $NH_2$ , - $C\equiv N$ , - $CF_3$ , or - $N_3$ ,

(II)  $-(CH_2)_{1-2}-S-CH_3$ ,

(III)  $-CH_2-CH_2-S-CH_3$ ,

(IV)  $-CH_2-(C_2-C_6 \text{ alkenyl})$  unsubstituted or substituted by one -F,

(V)  $-(CH_2)_{0-3}-(R_{1-aryl})$  where  $R_{1-aryl}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:

(A)  $C_1$ - $C_3$  alkyl,

(B)  $-CF_3$ ,

(C) -F, Cl, -Br and -I,

(D)  $C_1$ - $C_3$  alkoxy,

(E)  $-O-CF_3$ ,

(F)  $-NH_2$ ,

(G) -OH, or

(H)  $-C\equiv N$ ,

(VI)  $-(CH_2)_{n_1}-(R_{1-\text{heteroaryl}})$  where  $n_1$  is 0, 1, 2, or 3 and  $R_{1-\text{heteroaryl}}$  is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,

(BB) pyrrolyl,

(CC) oxadiazolyl,



(DD) thiadiazolyl,  
 (EE) triazolyl,  
 (FF) tetrazolyl,  
 (GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanlyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,
- (3)  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,
- (4)  $C_1$ - $C_3$  alkoxy,
- (5)  $-O-CF_3$ ,

(6)  $\text{-NH}_2$ ,

(7)  $\text{-OH}$ , or

(8)  $\text{-C}\equiv\text{N}$ ,

with the proviso that when  $n_1$  is zero  $\text{R}_{1\text{-heteroaryl}}$  is not bonded to the carbon chain by nitrogen, or

(VII)  $\text{-(CH}_2\text{)}_{n_1}\text{-(R}_{1\text{-heterocycle}}\text{)}$  where  $n_1$  is as defined above and

$\text{R}_{1\text{-heterocycle}}$  is:

(A) morpholinyl,

(B) thiomorpholinyl,

(C) thiomorpholinyl S-oxide,

(D) thiomorpholinyl S,S-dioxide,

(E) piperazinyl,

(F) homopiperazinyl,

(G) pyrrolidinyl,

(H) pyrrolinyl,

(I) tetrahydropyranyl,

(J) piperidinyl,

(K) tetrahydrofuranyl, or

(L) tetrahydrothiophenyl,

where the  $\text{R}_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $\text{R}_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $\text{R}_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

(1)  $\text{=O}$ ,

(2)  $\text{C}_1\text{-C}_3$  alkyl,

(3)  $\text{-CF}_3$ ,

(4)  $\text{-F}$ ,  $\text{Cl}$ ,  $\text{-Br}$  and  $\text{-I}$ ,

(5)  $\text{C}_1\text{-C}_3$  alkoxy,

(6)  $\text{-O-CF}_3$ ,

(7)  $\text{-NH}_2$ ,

(8)  $\text{-OH}$ , or

(9)  $-\text{C}\equiv\text{N}$ ,

with the proviso that when  $n_1$  is zero  $\text{R}_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $\text{R}_2$  is:

(I)  $-\text{H}$ ,

(II)  $\text{C}_1\text{-C}_6$  alkyl, or

(III)  $-(\text{CH}_2)_{0-4}\text{-R}_{2-1}$  where  $\text{R}_{2-1}$  is  $(\text{C}_3\text{-C}_6)\text{cycloalkyl}$ ,  $\text{R}_{1\text{-aryl}}$  or  $\text{R}_{1\text{-heteroaryl}}$

where  $\text{R}_{1\text{-aryl}}$  and  $\text{R}_{1\text{-heteroaryl}}$  are as defined above,

where  $\text{R}_N$  is:

(I)  $\text{R}_{N-1}\text{-X}_N$  where  $\text{X}_N$  is:

(A)  $-\text{CO}-$ ,

(B)  $-\text{SO}_2-$ ,

(C)  $-(\text{CR}'\text{R}'')_{1-6}$  where  $\text{R}'$  and  $\text{R}''$  are the same or different and are  $-\text{H}$  or  $\text{C}_1\text{-C}_4$  alkyl,

(D)  $-\text{CO}-(\text{CR}'\text{R}'')_{1-6}\text{-X}_{N-1}$  where  $\text{X}_{N-1}$  is  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'\text{R}''-$  and where  $\text{R}'$  and  $\text{R}''$  are as defined above,

(E) a single bond;

where  $\text{R}_{N-1}$  is:

(A)  $\text{R}_{N\text{-aryl}}$  where  $\text{R}_{N\text{-aryl}}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1)  $\text{C}_1\text{-C}_6$  alkyl,

(2)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

(3)  $-\text{OH}$ ,

(4)  $-\text{NO}_2$ ,

(5)  $-\text{CO-OH}$ ,

(6)  $-\text{C}\equiv\text{N}$ ,

(7)  $-\text{CO-NR}_{N-2}\text{R}_{N-3}$  where  $\text{R}_{N-2}$  and  $\text{R}_{N-3}$  are the same or different and are:

(a)  $-\text{H}$ ,



- (17)  $\text{-NH-CO-O-R}_{N-5}$  where  $R_{N-5}$  is as defined above,
- (18)  $\text{-NH-CO-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (19)  $\text{-N-CS-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (20)  $\text{-N(C}_1\text{-C}_3\text{ alkyl)-CO-R}_{N-5}$  where  $R_{N-5}$  is as defined above,
- (21)  $\text{-NR}_{N-2}\text{R}_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,
- (22)  $\text{-R}_{N-4}$  where  $R_{N-4}$  is as defined above,
- (23)  $\text{-O-CO-(C}_1\text{-C}_6\text{ alkyl)}$ ,
- (24)  $\text{-O-CO-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (25)  $\text{-O-CS-N(C}_1\text{-C}_3\text{ alkyl)}_2$ ,
- (26)  $\text{-O-(C}_1\text{-C}_6\text{ alkyl)}$ ,
- (27)  $\text{-O-(C}_2\text{-C}_5\text{ alkyl)-COOH}$ ,
- (28)  $\text{-S-(C}_1\text{-C}_6\text{ alkyl)}$ ,
- (29)  $\text{C}_1\text{-C}_6$  alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5  $\text{-F}$ ,
- (30)  $\text{-O-(C}_1\text{-C}_6\text{ alkyl)}$  unsubstituted or substituted with 1, 2, 3, 4, or 5  $\text{-F}$ , or
- (31)  $\text{-O-}\phi$ ,

(B)  $\text{-R}_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,

(L) isoquinolyl,  
(M) quinazolinyI,  
(N) quinoxalinyI,  
(O) phthalazinyI,  
(P) imidazolyl,  
(Q) isoxazolyl,  
(R) pyrazolyl,  
(S) oxazolyl,  
(T) thiazolyl,  
(U) indolizinyI,  
(V) indazolyl,  
(W) benzothiazolyl,  
(X) benzimidazolyl,  
(Y) benzofuranyl,  
(Z) furanyl,  
(AA) thienyl,  
(BB) pyrrolyl,  
(CC) oxadiazolyl,  
(DD) thiadiazolyl,  
(EE) triazolyl,  
(FF) tetrazolyl,  
(GG) 1, 4-benzodioxan  
(HH) purinyI,  
(II) oxazolopyridinyI,  
(JJ) imidazopyridinyI,  
(KK) isothiazolyl,  
(LL) naphthyridinyI,  
(MM) cinnolinyI,  
(NN) carbazolyl,  
(OO)  $\beta$ -carbolinyI,  
(PP) isochromanyI,

(QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1\text{-}C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b)  $C_1\text{-}C_6$  alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,
  - (c)  $C_1\text{-}C_6$  alkyl unsubstituted or substituted with 1, 2, or 3 -F, -Cl, -Br, or -I,
  - (d)  $C_3\text{-}C_7$  cycloalkyl,
  - (e)  $(C_1\text{-}C_2 \text{ alkyl})\text{-}(C_3\text{-}C_7 \text{ cycloalkyl})$ ,
  - (f)  $(C_1\text{-}C_6 \text{ alkyl})\text{-O}\text{-}(C_1\text{-}C_3 \text{ alkyl})$ ,

(g)  $-C_1-C_6$  alkenyl with one or two double bonds,

(h)  $-C_1-C_6$  alkynyl with one or two triple bonds,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,  
or

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(8)  $-CO-(C_3-C_{12} \text{ alkyl})$ ,

(9)  $-CO-(C_3-C_6 \text{ cycloalkyl})$ ,

(10)  $-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(11)  $-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,

(12)  $-CO-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3$  alkyl,

(13)  $-CO-O-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $C_1-C_6$  alkyl, or

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,

(14)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

(15)  $-SO-(C_1-C_8 \text{ alkyl})$ ,

(16)  $-SO_2-(C_3-C_{12} \text{ alkyl})$ ,

(17)  $-NH-CO-O-R_{N-5}$  where  $R_{N-5}$  is as defined above,

(18)  $-NH-CO-N(C_1-C_3 \text{ alkyl})_2$ ,



- (19)  $-N-CS-N(C_1-C_3 \text{ alkyl})_2$ ,  
 (20)  $-N(C_1-C_3 \text{ alkyl})-CO-R_{N-5}$  where  $R_{N-5}$  is as defined above,  
 (21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,  
 (22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,  
 (23)  $-O-CO-(C_1-C_6 \text{ alkyl})$ ,  
 (24)  $-O-CO-N(C_1-C_3 \text{ alkyl})_2$ ,  
 (25)  $-O-CS-N(C_1-C_3 \text{ alkyl})_2$ ,  
 (26)  $-O-(C_1-C_6 \text{ alkyl})$ ,  
 (27)  $-O-(C_2-C_5 \text{ alkyl})-COOH$ , or  
 (28)  $-S-(C_1-C_6 \text{ alkyl})$ ,

- (C)  $-R_{N-aryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,  
 (D)  $-R_{N-aryl}-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,  
 (E)  $-R_{N-heteroaryl}-R_{N-aryl}$  where  $-R_{N-aryl}$  and  $-R_{N-heteroaryl}$  are as defined above,  
 (F)  $-R_{N-heteroaryl}-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,  
 (G)  $-R_{N-aryl}-O-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,  
 (H)  $-R_{N-aryl}-S-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,  
 (I)  $-R_{N-heteroaryl}-O-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,  
 (J)  $-R_{N-heteroaryl}-S-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,  
 (K)  $-R_{N-aryl}-CO-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,  
 (L)  $-R_{N-aryl}-CO-R_{N-heteroaryl}$  where  $-R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above,  
 (M)  $-R_{N-aryl}-SO_2-R_{N-aryl}$  where  $-R_{N-aryl}$  is as defined above,  
 (N)  $-R_{N-heteroaryl}-CO-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,  
 (O)  $-R_{N-heteroaryl}-SO_2-R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above,  
 (P)  $-R_{N-aryl}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N-aryl}$  is as defined above,

(Q)  $-R_{N\text{-aryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,

(R)  $-R_{N\text{-heteroaryl}}-O-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or

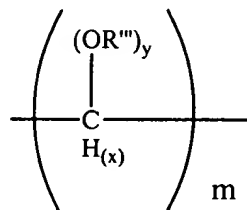
(S)  $-R_{N\text{-heteroaryl}}-S-(C_1-C_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $A-X_N-$  where  $X_N$  is  $-\text{CO}-$ ,

wherein A is

(A)  $-T-E-(Q)_{m'}$ ,

(1) where  $-T$  is



where

(a)  $x = 1$  when  $y = 1$  and  $x = 2$  when  $y = 0$ ,

(b)  $m$  is 0, 1, 2 or 3,

(c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and

(d)  $R'''$  varies independently on each carbon and is H,  $(C_1-C_2)$  alkyl, phenyl, or phenyl $(C_1-C_3)$ alkyl;

(2)  $-E$  is

(a)  $C_1-C_5$  alkyl, but only if  $m'$  does not equal 0,

(b) methylthioxy $(C_2-C_4)$ alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -E(Q)<sub>m''</sub> wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) -CO-(C<sub>1</sub>-C<sub>6</sub> alkyl) where alkyl is unsubstituted or substituted with one or two:

(A) -OH,

(B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,

(C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,

(D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,

(E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,

(K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub> is the same or different and are as defined above, or

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(IV) -CO-(C<sub>1</sub>-C<sub>3</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,

(C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,

(D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -φ,

(E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$  are the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,
- (V)  $-\text{CO}-(\text{C}_1-\text{C}_3 \text{ alkyl})-\text{S}-(\text{C}_1-\text{C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,
- (K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(N)  $-O-CO-NR_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or

(O)  $-O-(C_1-C_5 \text{ alkyl})-COOH$ ,

(VI)  $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-R_{N-aryl}/R_{N-heteroaryl}$  where  $R_{N-aryl}$  and  $R_{N-heteroaryl}$  are as defined above, where  $R_{N-10}$  is:

(A)  $-H$ ,

(B)  $C_1-C_6$  alkyl,

(C)  $C_3-C_7$  cycloalkyl,

(D)  $C_2-C_6$  alkenyl with one double bond,

(E)  $C_2-C_6$  alkynyl with one triple bond,

(F)  $R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, or

(G)  $R_{N-heteroaryl}$  where  $R_{N-heteroaryl}$  is as defined above;

where B is  $-O-$ ,  $-NH-$ , or  $-N(C_1-C_6 \text{ alkyl})-$ ;

where  $R_C$  is:

(I)  $-(C_1-C_{10})\text{alkyl}-K_{1-3}$  in which:

(A) the alkyl chain is unsubstituted or substituted with one  $-OH$ ,

(B) the alkyl chain is unsubstituted or substituted with one  $C_1-C_6$  alkoxy unsubstituted or substituted with 1-5  $-F$ ,

(C) the alkyl chain is unsubstituted or substituted with one  $-O-\phi$ ,

(D) the alkyl chain is unsubstituted or substituted with 1-5  $-F$ ,

(E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,

(F) each K is:

(1)  $H$ ,

(2)  $C_1-C_3$  alkyl,

(3)  $C_1-C_3$  alkoxy,

(4)  $C_1-C_3$  alkylthioxy,

(5)  $C_1-C_6$  alkylacylamino,

(6)  $C_1-C_6$  alkylacyloxy,

- (7) amido
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II) -(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,
- (B) -CO-OH,
- (C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),
- (D) -OH, or
- (E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(IV) -(CH<sub>2</sub>)<sub>2-6</sub>-OH,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are -H, C<sub>1</sub>-C<sub>4</sub> alkyl and  $\phi$ - and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub>,

(VI)  $-(CH_2)_{0-4}-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) isoxazolyl,
- (Q) pyrazolyl,
- (R) indolizinyl,
- (S) indazolyl,
- (T) benzothiazolyl,
- (U) benzimidazolyl,
- (V) benzofuranyl,
- (W) furanyl,
- (X) thienyl,
- (Y) pyrrolyl,
- (Z) oxadiazolyl,
- (AA) thiadiazolyl,
- (BB) triazolyl,
- (CC) tetrazolyl,
- (DD) 1, 4-benzodioxan

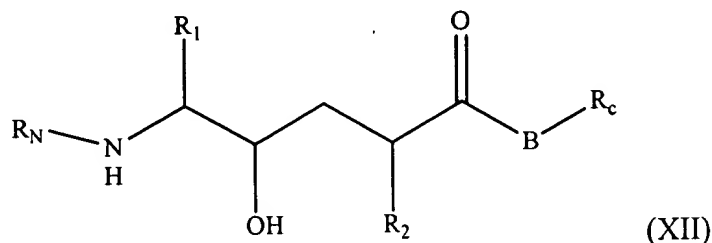


- (EE) purinyl,
- (FF) oxazolopyridinyl,
- (GG) imidazopyridinyl,
- (HH) isothiazolyl,
- (II) naphthyridinyl,
- (JJ) cinnolinyl,
- (KK) carbazolyl,
- (LL)  $\beta$ -carbolinyl,
- (MM) isochromanyl,
- (NN) chromanyl,
- (OO) furazanyl,
- (PP) tetrahydroisoquinoline,
- (QQ) isoindolinyl,
- (RR) isobenzotetrahydrofuranyl,
- (SS) isobenzotetrahydrothienyl,
- (TT) isobenzothiophenyl,
- (UU) benzoxazolyl, or
- (VV) pyridopyridinyl,
- (VII)  $-(CH_2)_{0-4}-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is the same as  $R_{1-heterocycle}$ ,
- (VIII)  $-C(R_{C-1})(R_{C-2})-CO-NH-R_{C-3}$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are:
  - (A) -H,
  - (B)  $-C_1-C_6$  alkyl,
  - (C)  $-(C_1-C_4 \text{ alkyl})-R_{C'-aryl}$  where  $R_{C'-aryl}$  is as defined above for  $R_{1-aryl}$ ,
  - (D)  $-(C_1-C_4 \text{ alkyl})-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
  - (E)  $-(C_1-C_4 \text{ alkyl})-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
  - (F)  $-R_{C-heteroaryl}$  where  $R_{C-heteroaryl}$  is as defined above,
  - (G)  $-R_{C-heterocycle}$  where  $R_{C-heterocycle}$  is as defined above,
  - (H)  $-(CH_2)_{1-4}-OH$ ,



- (A)  $-\text{OH}$ , or  
 (B)  $-\text{CH}_2-\text{OH}$ ;  
 (XIII)  $-\text{CH}(-\phi)-\text{CO}-\text{O}(\text{C}_1-\text{C}_3 \text{ alkyl})$ ;  
 (XIV)  $-\text{CH}(-\text{CH}_2-\text{OH})-\text{CH}(-\text{OH})-\phi-\text{NO}_2$ ;  
 (XV)  $-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{OH}$ ;  
 (XVI)  $-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}(-\text{O}-\text{CH}_2-\text{CH}_3)_2$ ;  
 (XVII)  $-(\text{C}_2-\text{C}_8) \text{ alkynyl}$ ; or  
 (XVIII)  $-\text{H}$ ; or a pharmaceutically acceptable salt thereof.

61. A method for producing a  $\beta$ -secretase complex comprising exposing  $\beta$ -secretase to a hydroxyethylene compound of the formula



where  $\text{R}_1$  is:

- (I)  $\text{C}_1-\text{C}_6$  alkyl, unsubstituted or substituted with one, two or three  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{NH}_2$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ , or  $-\text{N}_3$ ,  
 (II)  $-(\text{CH}_2)_{1-2}-\text{S}-\text{CH}_3$ ,  
 (III)  $-\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_3$ ,  
 (IV)  $-\text{CH}_2-(\text{C}_2-\text{C}_6 \text{ alkenyl})$  unsubstituted or substituted by one  $-\text{F}$ ,  
 (V)  $-(\text{CH}_2)_{0-3}-(\text{R}_{1-\text{aryl}})$  where  $\text{R}_{1-\text{aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of the following substituents which can be the same or different:  
 (A)  $\text{C}_1-\text{C}_3$  alkyl,  
 (B)  $-\text{CF}_3$ ,  
 (C)  $-\text{F}$ ,  $\text{Cl}$ ,  $-\text{Br}$  and  $-\text{I}$ ,  
 (D)  $\text{C}_1-\text{C}_3$  alkoxy,

(E)  $-\text{O}-\text{CF}_3$ ,

(F)  $-\text{NH}_2$ ,

(G)  $-\text{OH}$ , or

(H)  $-\text{C}\equiv\text{N}$ ,

(VI)  $-(\text{CH}_2)_{n_1}-(\text{R}_{1-\text{heteroaryl}})$  where  $n_1$  is 0, 1, 2, or 3 and  $\text{R}_{1-\text{heteroaryl}}$  is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) imidazolyl,

(Q) isoxazolyl,

(R) pyrazolyl,

(S) oxazolyl,

(T) thiazolyl,

(U) indolizinyl,

(V) indazolyl,

(W) benzothiazolyl,

(X) benzimidazolyl,

(Y) benzofuranyl,

(Z) furanyl,

(AA) thienyl,  
 (BB) pyrrolyl,  
 (CC) oxadiazolyl,  
 (DD) thiadiazolyl,  
 (EE) triazolyl,  
 (FF) tetrazolyl,  
 (GG) 1, 4-benzodioxan  
 (HH) purinyl,  
 (II) oxazolopyridinyl,  
 (JJ) imidazopyridinyl,  
 (KK) isothiazolyl,  
 (LL) naphthyridinyl,  
 (MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{0-3}-$  by any ring atom of the parent  $R_N$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_3$  alkyl,
- (2)  $-CF_3$ ,

- (3) -F, Cl, -Br, or -I,
- (4) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (5) -O-CF<sub>3</sub>,
- (6) -NH<sub>2</sub>,
- (7) -OH, or
- (8) -C≡N,

with the proviso that when n<sub>1</sub> is zero R<sub>1-heteroaryl</sub> is not bonded to the carbon chain by nitrogen, or

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heterocycle</sub>) where n<sub>1</sub> is as defined above and

R<sub>1-heterocycle</sub> is:

- (A) morpholinyl,
- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

where the R<sub>1-heterocycle</sub> group is bonded by any atom of the parent R<sub>1-heterocycle</sub> group substituted by hydrogen such that the new bond to the R<sub>1-heteroaryl</sub> group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) -CF<sub>3</sub>,
- (4) -F, Cl, -Br and -I,
- (5) C<sub>1</sub>-C<sub>3</sub> alkoxy,

(6)  $-\text{O}-\text{CF}_3$ ,

(7)  $-\text{NH}_2$ ,

(8)  $-\text{OH}$ , or

(9)  $-\text{C}\equiv\text{N}$ ,

with the proviso that when  $n_1$  is zero  $\text{R}_{1\text{-heterocycle}}$  is not bonded to the carbon chain by nitrogen;

where  $\text{R}_2$  is:

(I)  $-\text{H}$ ,

(II)  $\text{C}_1\text{-C}_6$  alkyl, or

(III)  $-(\text{CH}_2)_{0-4}-\text{R}_{2-1}$  where  $\text{R}_{2-1}$  is  $(\text{C}_3\text{-C}_6)\text{cycloalkyl}$ ,  $\text{R}_{1\text{-aryl}}$  or  $\text{R}_{1\text{-heteroaryl}}$

where  $\text{R}_{1\text{-aryl}}$  and  $\text{R}_{1\text{-heteroaryl}}$  are as defined above,

where  $\text{R}_N$  is:

(I)  $\text{R}_{N-1}-\text{X}_N$  where  $\text{X}_N$  is:

(A)  $-\text{CO}-$ ,

(B)  $-\text{SO}_2-$ ,

(C)  $-(\text{CR}'\text{R}'')_{1-6}$  where  $\text{R}'$  and  $\text{R}''$  are the same or different and are  $-\text{H}$  or  $\text{C}_1\text{-C}_4$  alkyl,

(D)  $-\text{CO}-(\text{CR}'\text{R}'')_{1-6}-\text{X}_{N-1}$  where  $\text{X}_{N-1}$  is  $-\text{O}-$ ,  $-\text{S}-$  and  $-\text{NR}'\text{R}''$  and where  $\text{R}'$  and  $\text{R}''$  are as defined above,

(E) a single bond;

where  $\text{R}_{N-1}$  is:

(A)  $\text{R}_{N\text{-aryl}}$  where  $\text{R}_{N\text{-aryl}}$  is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

(1)  $\text{C}_1\text{-C}_6$  alkyl,

(2)  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

(3)  $-\text{OH}$ ,

(4)  $-\text{NO}_2$ ,

(5)  $-\text{CO}-\text{OH}$ ,

(6)  $-\text{C}\equiv\text{N}$ ,

(7)  $-\text{CO}-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are:

(a)  $-\text{H}$ ,

(b)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one

(i)  $-\text{OH}$ , or

(ii)  $-\text{NH}_2$ ,

(c)  $-\text{C}_1-\text{C}_6$  alkyl unsubstituted or substituted with one to three  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

(d)  $-\text{C}_3-\text{C}_7$  cycloalkyl,

(e)  $-(\text{C}_1-\text{C}_2 \text{ alkyl})-(\text{C}_3-\text{C}_7 \text{ cycloalkyl})$ ,

(f)  $-(\text{C}_1-\text{C}_6 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_3 \text{ alkyl})$ ,

(g)  $-\text{C}_1-\text{C}_6$  alkenyl with one or two double bonds,

(h)  $-\text{C}_1-\text{C}_6$  alkynyl with one or two triple bonds,

(i)  $-\text{C}_1-\text{C}_6$  alkyl chain with one double bond and one triple bond,

(j)  $-\text{R}_{1-\text{aryl}}$  where  $\text{R}_{1-\text{aryl}}$  is as defined above, or

(k)  $-\text{R}_{1-\text{heteroaryl}}$  where  $\text{R}_{1-\text{heteroaryl}}$  is as defined above,

(8)  $-\text{CO}-(\text{C}_3-\text{C}_{12} \text{ alkyl})$ ,

(9)  $-\text{CO}-(\text{C}_3-\text{C}_6 \text{ cycloalkyl})$ ,

(10)  $-\text{CO}-\text{R}_{1-\text{heteroaryl}}$  where  $\text{R}_{1-\text{heteroaryl}}$  is as defined above,

(11)  $-\text{CO}-\text{R}_{1-\text{heterocycle}}$  where  $\text{R}_{1-\text{heterocycle}}$  is as defined above,

(12)  $-\text{CO}-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $\text{C}_1-\text{C}_3$  alkyl,

(13)  $-\text{CO}-\text{O}-\text{R}_{\text{N}-5}$  where  $\text{R}_{\text{N}-5}$  is:

(a)  $\text{C}_1-\text{C}_6$  alkyl, or

(b)  $-(\text{CH}_2)_{0-2}-(\text{R}_{1-\text{aryl}})$  where  $\text{R}_{1-\text{aryl}}$  is as defined above,





- (H) indolinyI,
- (I) pyridazinyI,
- (J) pyrazinyI,
- (K) isoindolyI,
- (L) isoquinolyI,
- (M) quinazolinyl,
- (N) quinoxalinyI,
- (O) phthalazinyI,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyI,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thienyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,
- (GG) 1, 4-benzodioxan
- (HH) purinyI,
- (II) oxazolopyridinyI,
- (JJ) imidazopyridinyI,
- (KK) isothiazolyl,
- (LL) naphthyridinyI,

(MM) cinnolinyl,  
 (NN) carbazolyl,  
 (OO)  $\beta$ -carbolinyl,  
 (PP) isochromanyl,  
 (QQ) chromanyl,  
 (RR) furazanyl,  
 (SS) tetrahydroisoquinoline,  
 (TT) isoindolinyl,  
 (UU) isobenzotetrahydrofuranyl,  
 (VV) isobenzotetrahydrothienyl,  
 (WW) isobenzothiophenyl,  
 (XX) benzoxazolyl, or  
 (YY) pyridopyridinyl,

where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1)  $C_1$ - $C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C $\equiv$ N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b) - $C_1$ - $C_6$  alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,

(c)  $-C_1-C_6$  alkyl unsubstituted or substituted with 1, 2, or 3  $-F$ ,  $-Cl$ ,  $-Br$ , or  $-I$ ,

(d)  $-C_3-C_7$  cycloalkyl,

(e)  $-(C_1-C_2 \text{ alkyl})-(C_3-C_7 \text{ cycloalkyl})$ ,

(f)  $-(C_1-C_6 \text{ alkyl})-O-(C_1-C_3 \text{ alkyl})$ ,

(g)  $-C_1-C_6$  alkenyl with one or two double bonds,

(h)  $-C_1-C_6$  alkynyl with one or two triple bonds,

(i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,

(j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,  
or

(k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(8)  $-CO-(C_3-C_{12} \text{ alkyl})$ ,

(9)  $-CO-(C_3-C_6 \text{ cycloalkyl})$ ,

(10)  $-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,

(11)  $-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,

(12)  $-CO-R_{N-4}$  where  $R_{N-4}$  is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two  $C_1-C_3$  alkyl,

(13)  $-CO-O-R_{N-5}$  where  $R_{N-5}$  is:

(a)  $C_1-C_6$  alkyl, or

(b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,

(14)  $-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,

- (15) -SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (16) -SO<sub>2</sub>-(C<sub>3</sub>-C<sub>12</sub> alkyl),
- (17) -NH-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,
- (18) -NH-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (19) -N-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (20) -N(C<sub>1</sub>-C<sub>3</sub> alkyl)-CO-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,
- (21) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or different and are as defined above,
- (22) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (23) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (24) -O-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (25) -O-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (26) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (27) -O-(C<sub>2</sub>-C<sub>5</sub> alkyl)-COOH, or
- (28) -S-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (C) -R<sub>N-aryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,
- (D) -R<sub>N-aryl</sub>-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,
- (E) -R<sub>N-heteroaryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,
- (F) -R<sub>N-heteroaryl</sub>-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,
- (G) -R<sub>N-aryl</sub>-O-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,
- (H) -R<sub>N-aryl</sub>-S-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,
- (I) -R<sub>N-heteroaryl</sub>-O-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,
- (J) -R<sub>N-heteroaryl</sub>-S-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,
- (K) -R<sub>N-aryl</sub>-CO-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,
- (L) -R<sub>N-aryl</sub>-CO-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and R<sub>N-heteroaryl</sub> are as defined above,
- (M) -R<sub>N-aryl</sub>-SO<sub>2</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(N)  $-R_{N\text{-heteroaryl}}-\text{CO}-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(O)  $-R_{N\text{-heteroaryl}}-\text{SO}_2-R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(P)  $-R_{N\text{-aryl}}-\text{O}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,

(Q)  $-R_{N\text{-aryl}}-\text{S}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-aryl}}$  is as defined above,

(R)  $-R_{N\text{-heteroaryl}}-\text{O}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above, or

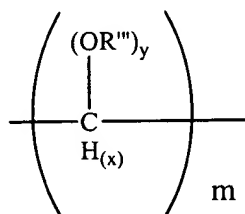
(S)  $-R_{N\text{-heteroaryl}}-\text{S}-(\text{C}_1\text{-C}_8 \text{ alkyl})-\phi$  where  $R_{N\text{-heteroaryl}}$  is as defined above,

(II)  $\text{A}-\text{X}_N$  where  $\text{X}_N$  is  $-\text{CO}-$ ,

wherein A is

(A)  $-\text{T}-\text{E}-(\text{Q})_{m'}$ ,

(1) where  $-\text{T}$  is



where

(a)  $x = 1$  when  $y = 1$  and  $x = 2$  when  $y = 0$ ,

(b)  $m$  is 0, 1, 2 or 3,

(c) the values of  $x$  and  $y$  vary independently on each carbon when  $m$  is 2 and 3, and

(d)  $\text{R}'''$  varies independently on each carbon and is H,  $(\text{C}_1\text{-C}_2)$  alkyl, phenyl, or phenyl $(\text{C}_1\text{-C}_3)$ alkyl;

(2)  $-\text{E}$  is

(a)  $\text{C}_1\text{-C}_5$  alkyl, but only if  $m'$  does not equal 0,

(b) methylthioxy $(\text{C}_2\text{-C}_4)$ alkyl,

- (c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,
- (e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,
- (f) biphenyl,
- (g) diphenyl ether,
- (h) diphenylketone,
- (i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or
- (j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

- (a) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (b) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

- (B)  $-E(Q)_m$  wherein E and -Q are as defined as above and m is 0, 1, 2, or 3;
- (C)  $-T-E$  wherein -E and -Q are as defined as above; or
- (D)  $-E$  wherein -E is as defined as above;

(III)  $-\text{CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two:

- (A)  $-\text{OH}$ ,
- (B)  $-\text{C}_1\text{-C}_6 \text{ alkoxy}$ ,
- (C)  $-\text{C}_1\text{-C}_6 \text{ thioalkoxy}$ ,
- (D)  $-\text{CO-O-R}_{N-8}$  where  $R_{N-8}$  is  $-\text{H}$ ,  $\text{C}_1\text{-C}_6 \text{ alkyl}$  or  $-\phi$ ,
- (E)  $-\text{CO-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (F)  $-\text{CO-R}_{N-4}$  where  $R_{N-4}$  is as defined above,
- (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (I)  $-\text{NH-CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (J)  $-\text{NH-CO-O-R}_{N-8}$  where  $R_{N-8}$  is as defined above,
- (K)  $-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{N-4}$  where  $R_{N-4}$  is as defined above,
- (M)  $-\text{O-CO}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O-CO-NR}_{N-8}R_{N-8}$  where the  $R_{N-8}$  is the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1\text{-C}_5 \text{ alkyl})\text{-COOH}$ ,

(IV)  $-\text{CO}-(\text{C}_1\text{-C}_3 \text{ alkyl})\text{-O}-(\text{C}_1\text{-C}_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two

- (A)  $-\text{OH}$ ,



- (B)  $-C_1-C_6$  alkoxy,
- (C)  $-C_1-C_6$  thioalkoxy,
- (D)  $-\text{CO}-\text{O}-R_{N-8}$  where  $R_{N-8}$  is  $-\text{H}$ ,  $C_1-C_6$  alkyl or  $-\phi$ ,
- (E)  $-\text{CO}-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (F)  $-\text{CO}-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (G)  $-\text{SO}_2-(C_1-C_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (I)  $-\text{NH}-\text{CO}-(C_1-C_6 \text{ alkyl})$ ,
- (J)  $-\text{NH}-\text{CO}-\text{O}-R_{N-8}$  where  $R_{N-8}$  is as defined above,
- (K)  $-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
- (L)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(C_1-C_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{N-8}R_{N-8}$  where the  $R_{N-8}$  are the same or different and are as defined above, or
- (O)  $-\text{O}-(C_1-C_5 \text{ alkyl})-\text{COOH}$ ,
- (V)  $-\text{CO}-(C_1-C_3 \text{ alkyl})-\text{S}-(C_1-C_3 \text{ alkyl})$  where alkyl is unsubstituted or substituted with one or two
  - (A)  $-\text{OH}$ ,
  - (B)  $-C_1-C_6$  alkoxy,
  - (C)  $-C_1-C_6$  thioalkoxy,
  - (D)  $-\text{CO}-\text{O}-R_{N-8}$  where  $R_{N-8}$  is  $-\text{H}$ ,  $C_1-C_6$  alkyl or  $-\phi$ ,
  - (E)  $-\text{CO}-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
  - (F)  $-\text{CO}-R_{N-4}$  where  $R_{N-4}$  is as defined above,
  - (G)  $-\text{SO}_2-(C_1-C_8 \text{ alkyl})$ ,
  - (H)  $-\text{SO}_2-\text{NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,
  - (I)  $-\text{NH}-\text{CO}-(C_1-C_6 \text{ alkyl})$ ,

- (J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is as defined above,
- (K)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
- (M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,
- (N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N}-8}\text{R}_{\text{N}-8}$  where the  $\text{R}_{\text{N}-8}$  are the same or different and are as defined above, or
- (O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,
- (VI)  $-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{\text{N}-10})-(\text{CH}_2)_{0-2}-\text{R}_{\text{N-aryl}}/\text{R}_{\text{N-heteroaryl}}$  where  $\text{R}_{\text{N-aryl}}$  and  $\text{R}_{\text{N-heteroaryl}}$  are as defined above, where  $\text{R}_{\text{N}-10}$  is:
- (A)  $-\text{H}$ ,
- (B)  $\text{C}_1-\text{C}_6 \text{ alkyl}$ ,
- (C)  $\text{C}_3-\text{C}_7 \text{ cycloalkyl}$ ,
- (D)  $\text{C}_2-\text{C}_6 \text{ alkenyl}$  with one double bond,
- (E)  $\text{C}_2-\text{C}_6 \text{ alkynyl}$  with one triple bond,
- (F)  $\text{R}_{1\text{-aryl}}$  where  $\text{R}_{1\text{-aryl}}$  is as defined above, or
- (G)  $\text{R}_{\text{N-heteroaryl}}$  where  $\text{R}_{\text{N-heteroaryl}}$  is as defined above;

where B is  $-\text{O}-$ ,  $-\text{NH}-$ , or  $-\text{N}(\text{C}_1-\text{C}_6 \text{ alkyl})-$ ;

where  $\text{R}_\text{C}$  is:

- (I)  $-(\text{C}_1-\text{C}_{10})\text{alkyl}-\text{K}_{1-3}$  in which:
- (A) the alkyl chain is unsubstituted or substituted with one  $-\text{OH}$ ,
- (B) the alkyl chain is unsubstituted or substituted with one  $\text{C}_1-\text{C}_6$  alkoxy unsubstituted or substituted with 1-5  $-\text{F}$ ,
- (C) the alkyl chain is unsubstituted or substituted with one  $-\text{O}-\phi$ ,
- (D) the alkyl chain is unsubstituted or substituted with 1-5  $-\text{F}$ ,
- (E) the alkyl chain is unsubstituted or substituted with a combination of up to three atoms of oxygen and sulfur each such atom replacing one carbon,
- (F) each K is:
- (1)  $\text{H}$ ,

- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (4) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,
- (5) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (6) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (7) amido
- (8) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (9) phenylamino,
- (10) carbamyl
- (11) carboxyl
- (12) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (13) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (14) heterocyclylacyl,
- (15) heteroarylacyl,
- (16) amino unsubstituted or substituted with C<sub>1</sub>-C<sub>6</sub> alkyl,
- (17) hydroxyl, or
- (18) carboxyl methyl ester;

(II)-(CH<sub>2</sub>)<sub>0-3</sub>-J-[-(CH<sub>2</sub>)<sub>0-3</sub>-K]<sub>1-3</sub> where K is as defined above and J is:

- (A) a 5 to 7 atom monocyclic aryl group,
- (B) a 8 to 12 atom multicyclic aryl group,
- (C) a 5 to 7 atom heterocyclic group,
- (D) a 8 to 12 atom multicyclic heterocyclic group, or
- (E) a 5 to 10 atom monocyclic or multicyclic cycloalkyl group;

(III) -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F, -Cl, -Br, or -I,
- (B) -CO-OH,
- (C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(D) -OH, or

(E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

(IV) -(CH<sub>2</sub>)<sub>2-6</sub>-OH,

(V) -(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub> where R<sub>C-x</sub> and R<sub>C-y</sub> are -H, C<sub>1</sub>-C<sub>4</sub> alkyl and  $\phi$ -  
and R<sub>C-aryl</sub> is the same as R<sub>N-aryl</sub>,

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is:

(A) pyridinyl,

(B) pyrimidinyl,

(C) quinolinyl,

(D) indenyl,

(E) indanyl,

(F) benzothiophenyl,

(G) indolyl,

(H) indolinyl,

(I) pyridazinyl,

(J) pyrazinyl,

(K) isoindolyl,

(L) isoquinolyl,

(M) quinazolinyl,

(N) quinoxalinyl,

(O) phthalazinyl,

(P) isoxazolyl,

(Q) pyrazolyl,

(R) indolizinyl,

(S) indazolyl,

(T) benzothiazolyl,

(U) benzimidazolyl,

(V) benzofuranyl,

(W) furanyl,

(X) thienyl,

(Y) pyrrolyl,

(Z) oxadiazolyl,  
(AA) thiadiazolyl,  
(BB) triazolyl,  
(CC) tetrazolyl,  
(DD) 1, 4-benzodioxan  
(EE) purinyl,  
(FF) oxazolopyridinyl,  
(GG) imidazopyridinyl,  
(HH) isothiazolyl,  
(II) naphthyridinyl,  
(JJ) cinnolinyl,  
(KK) carbazolyl,  
(LL)  $\beta$ -carbolinyl,  
(MM) isochromanyl,  
(NN) chromanyl,  
(OO) furazanyl,  
(PP) tetrahydroisoquinoline,  
(QQ) isoindolinyl,  
(RR) isobenzotetrahydrofuranyl,  
(SS) isobenzotetrahydrothienyl,  
(TT) isobenzothiophenyl,  
(UU) benzoxazolyl, or  
(VV) pyridopyridinyl,

(VII)  $-(\text{CH}_2)_{0-4}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$  is the same as  $\text{R}_{\text{I-heterocycle}}$ ,

different and are:

(B) -C<sub>1</sub>-C<sub>6</sub> alkyl,

R<sub>1</sub>-aryl,

(E)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(F)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(G)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(H)  $-(CH_2)_{1-4}-OH$ ,

(I)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C'\text{-aryl}}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$ ,  $-NH-$  or  $-NHR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'\text{-aryl}}$  is as defined above,

(J)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{1-4}-R_{C\text{-heteroaryl}}$  where  $R_{C-4}$  and  $R_{C\text{-heteroaryl}}$  are as defined above, or

(K)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

and where  $R_{C-3}$  is:

(A)  $-H$ ,

(B)  $-C_1-C_6$  alkyl,

(C)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

(D)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(E)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(F)  $-(C_1-C_4 \text{ alkyl})-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

(G)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

or

(H)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(IX)  $-CH(\phi)_2$ ,

(X)  $-cyclopentyl$  or  $-cyclohexyl$  ring fused to a phenyl or heteroaryl ring where heteroaryl is as defined above and phenyl and heteroaryl are unsubstituted or substituted with one, two or three:

(A)  $C_1-C_3$  alkyl,

(B)  $-CF_3$ ,

(C)  $-F$ ,  $-Cl$ ,  $-Br$  and  $-I$ ,

(D)  $C_1-C_3$  alkoxy,

(E)  $-OCF_3$ ,

(F)  $-\text{NH}_2$ ,

(G)  $-\text{OH}$ , or

(H)  $-\text{C}\equiv\text{N}$ ,

(XI)  $-\text{CH}_2-\text{C}\equiv\text{CH}$ ;

(XII)  $-(\text{CH}_2)_{0-1}-\text{CHR}_{\text{C-5}}-(\text{CH}_2)_{0-1}-\phi$  where  $\text{R}_{\text{C-5}}$  is:

(A)  $-\text{OH}$ , or

(B)  $-\text{CH}_2-\text{OH}$ ;

(XIII)  $-\text{CH}(-\phi)-\text{CO}-\text{O}(\text{C}_1-\text{C}_3 \text{ alkyl})$ ;

(XIV)  $-\text{CH}(-\text{CH}_2-\text{OH})-\text{CH}(-\text{OH})-\phi-\text{NO}_2$ ;

(XV)  $-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{OH}$ ;

(XVI)  $-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}(-\text{O}-\text{CH}_2-\text{CH}_3)_2$ ;

(XVII)  $-(\text{C}_2-\text{C}_8) \text{ alkynyl}$ ; or

(XVIII)  $-\text{H}$ ; or a pharmaceutically acceptable salt thereof.

in a reaction mixture under conditions suitable for the production of said complex.

62. The method of claim 61, where said exposing is *in vitro*.

63. The method of claim 61, wherein said reaction mixture is a cell.